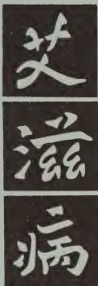


T H E S A N F O R D



GUIDE TO HIV/AIDS THERAPY

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COVER DESIGN: Chinese for 'AIDS'

(Translation courtesy Evelyn Cross, cover design by Nancy Sanford)

PREFACE: The genesis of this *Guide to HIV/AIDS* began in 1981 with the initial recognition of clusters of seemingly unusual infections (*Pneumocystis carinii* pneumonia) and malignancies (Kaposi's sarcoma) in young homosexual men in San Francisco and New York. It quickly became apparent that this was not an isolated occurrence but rather was the harbinger of a worldwide pandemic which would ultimately have major sociopolitical as well as medical impact. Recommendations for the management of the opportunistic infections in this condition (subsequently designated the acquired immunodeficiency syndrome) were included in the 1982 *Guide to Antimicrobial Therapy*. In 1988, Drs. Sande, Gerberding and Gilbert joined Dr. Sanford in updating the *Guide to Antimicrobial Therapy*. Over the past five years, we have added progressively more material on HIV infection/disease and the associated opportunistic infections to the *Guide*; however, the information was not organized specifically to assist the physician in the management of the AIDS patient. With the progression of the epidemic, most physicians have now become involved in the counseling or care of these patients. HIV infection is no longer a disease managed solely by the infectious disease specialist. To assist those health care providers who find it difficult if not impossible to keep abreast of the rapidly accumulating knowledge, we have undertaken to review, evaluate and compile the current state of knowledge in a summary fashion. This is not a textbook on HIV/AIDS, it is a *Guide* to assist the physician and ultimately the patient. The recommendations are based both on the literature and on personal experience, especially that from San Francisco General Hospital. As new information becomes available, many of these recommendations will change. It is important to recognize that the management of HIV infection and disease is constantly changing as new data are developed and reported. This *Guide* is current as of 1 June 1994. In view of the rapidity of change, a 1995 revision is envisioned.

We thank our many colleagues for sharing their knowledge and experience with us, especially those at San Francisco General Hospital. We are appreciative that they and many publishers have allowed us to adapt and in some instances reproduce material from other publications.

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Where recommendations suggest use of agents for purposes or in dosages other than those in product labeling, we have attempted to identify them as such.

This *Guide* is not being prepared for any single pharmaceutical company or distributor. It has not been subject to any form of approval prior to publication.

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**THE SANFORD
GUIDE TO
HIV/AIDS THERAPY
1994**

July 1994–July 1995

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ASSESSMENT OF HIV INFECTION RISKS AND RECOMMENDATIONS FOR HIV TESTING

I. General

HIV risk assessment is an essential component of primary care. In taking a history, avoid medical jargon (e.g., "intercourse"), vague terms ("sexually active"), group designations ("homosexual"), or judgmental terms ("promiscuous"). Learn the language and terminology understood and used by patients. Question responses to the depth necessary to elicit risky behavior and to define extent of risk of acquisition and transmission.

II. Specific Behaviors Associated With HIV Transmission

A. Sexual Behaviors

1. Sexual Partner(s)

- HIV-infected partners
- Partners who are at risk but have not been HIV tested (risk of HIV often underappreciated by partners)
- Multiple partners
- Presence of mucosal ulceration in either partner

2. Sexual Practices

a. High infection risk

- Unprotected anal receptive intercourse
- Unprotected vaginal receptive intercourse

b. Infection risk documented

- Unprotected oral receptive intercourse
- Unprotected anal insertive intercourse
- Unprotected vaginal insertive intercourse (risk may be higher during menses)
- Unprotected oral insertive intercourse

c. Lower infection risk

- Any of the above with latex/vinyl condom (vaginal or penile) protection. However, very few studies have been done to assess effectiveness of condoms in preventing HIV transmission. Based on contraceptive efficacy (97%) and defect rate (0.04%), effectiveness calculated as 8–27%/year (*J Sex Marital Therapy* 15:5, 1989). In 343 HIV+ women partners of HIV+ men, seroconversion for those who used condoms with every encounter was 1.1/100 person years while for those who used condoms intermittently or not at all, rate was 7.2/100 person years (*J AIDS* 6:497, 1993).
- Cunnilingus, especially with rubber dam, microwaveable plastic food wrap or other water-imperious barrier

d. Safer

- Deep kissing
- Protected sex with HIV test negative partner
- Mutual monogamy
- Mutual masturbation
- Masturbation or massage

e. Safest

- Abstinence

B. Injection (intravenous or "skin popping") Drug Use Behavior. Assess injectable anabolic steroid use! Assess sexual behaviors in all drug users!

Drug Use Practices:

1. Riskiest

- Sharing uncleaned needles, syringes, other paraphernalia (works), especially in "shooting galleries"
- Sharing drug contaminated by other users
- "Front loading" (passing drug from one syringe to another)

2. Less risky

- Sharing cleaned needles, syringes, works. (Household bleach is effective, especially after washing and when contact time is greater than 5 minutes. It is important to rinse with water after bleach use)
- Drug paraphernalia used repeatedly but by single user

3. Least risky

- Single use needles, syringes, works
- Sterile needles, syringes, works (needle/syringe exchange appears effective and has not increased drug use)

C. Blood Product Infusion Recipient

Blood Product Risks:

1. Riskiest
 - Receipt of multiple units of blood products between 1978-1985
 - Receipt of blood products obtained from donors in countries where screening is unreliable or not done
2. Less risky
 - Receipt of heterologous blood products in U.S. after 1985 (risk approximately 1:28,000 after an average of 5.4 units). [This is because of a window (about 8 weeks) between infection and seroconversion.] Rhogam and hepatitis B vaccine (serum-derived) have never been reported to transmit HIV-1.
 - Receipt of donor-selected blood products in U.S. after 1985 (but no safer than random donors)
3. Safest
 - Receipt of autologous blood products
 - Receipt of genetically engineered blood product substitutes

D. Perinatal Infection

1. General
 - a. Routine perinatal screening recommended in U.S., especially in high prevalence areas/populations
 - b. On 2/18/94 a placebo-controlled trial demonstrated that zidovudine prevented transmission of HIV from mother to infant. (See Table 10, page 81) (MMWR 43:285, 1994).
 - There has been no documentation of teratogenic effects related to zidovudine treatment (NEJM 326:857, 1992)
 - c. Diagnosis of infection in neonates remains problematic
 - All newborns of HIV+ mothers carry maternal HIV antibodies, sometimes as long as 15 months
 - Although overall transmission rate in U.S. is 15-30%, only 1/3 of infected children are virus + by any test at birth
 - "Almost all" HIV-infected infants can now be diagnosed by 6 months of age by one or a combination of: culture, polymerase-chain reaction (PCR), serologic detection of p24 antigen or branched HIV DNA assay (Rep Ped ID 3:3, 1993) (see Table 2, pages 6-7).
2. Relative risk determinants
 - a. Highest risk
 - Newborn of HIV+ mother who has delivered a previously infected child (risk > 50%)
 - b. At risk
 - Newborn of HIV+ mother (risk varies 15-60%)
 - No evidence delivery method (C-section) alters risk
 - Newborn of mother with unrecognized risk in partners
 - Breast-fed newborn of HIV+ mother
 - c. Lowest risk
 - Mother with negative HIV test

E. Occupational Exposure (See Table 16, page 95)

Relative Risk Determinants:

1. Riskiest (risk may be decreased by glove use, which removes > 50% blood from exposure site in some studies)
 - Parenteral inoculation via hollow needle of blood from source with advanced HIV disease or high titer viremia
 - Parenteral inoculation of materials containing high titer virus in research laboratory setting
2. Less risky
 - Small volume exposure via non-hollow needle
 - Mucosal exposure/non-intact skin exposure [risk is too low to be quantified in prospective studies; not zero but estimated to be at least a log (90%) lower than needlestick risk. Risk may be increased if large volume or prolonged contact occurs]
3. Risk not identified
 - Cutaneous contact (intact skin)
 - Exposure to urine, saliva, sweat, tears

F. Donor Organ or Tissue Transplantation

1. Test potential donors for HIV (note "window" between infection and seroconversion (C.2 above))
2. Assess donors for risk factors
3. Evaluate risk/benefits

III. Recommendations for HIV Testing

- A. HIV pre-test counseling should be provided to **all persons at risk** and HIV testing recommended. All who consent should be tested unless medically or psychiatrically contraindicated. Use pre-test counseling to encourage reduction of risk for acquisition and/or transmission (Examples: "What do you expect your test results to be? Why? What will you do if you are HIV+? Is there anything different you will do if you are HIV-?").
- B. "At Risk" Persons May Include:
1. All persons (men and women) with identified risk behaviors
 2. All persons with sexually transmitted diseases
 3. All persons with conditions associated with HIV infection (see Table 3, page 10)
 4. All persons with tuberculosis (among patients seen in TB clinics in 1988-1989, 3.4% (range 0-46%) were HIV+ (*J Inf Dis* 165:87, 1992))
 5. Pregnant women in areas of high prevalence
 6. Women of childbearing age in areas of high prevalence
 7. All patients, age 15-54 years, in-patient or out-patient, receiving care in institutions where HIV prevalence is $\geq 1\%$ or AIDS diagnosis rate is ≥ 1.0 per 1000 discharges (*MMWR* 42:(RR-2), 1993 (Jan. 15)). Such screening would involve only 593 of the 5558 U.S. Acute Care Hospitals and 12% of all patients but would detect 68% of HIV+ patients hospitalized for conditions other than symptomatic HIV disease (*NEJM* 327:445, 1992). For guidelines regarding the conduct of blinded HIV serosurveys in hospitals, contact Seroepidemiology Branch, Mail Stop E-46, CDC, Atlanta, GA 30333.
- C. Post-Test Counseling: Provide test results preferably in person, assess mental status, review risk reduction/third-party risks (see II.A,B above), provide follow-up referral.

TABLE 2
DIAGNOSTIC TESTS
for HIV-1, HIV-2, HTLV-I, HTLV-II, and Idiopathic CD4 T-Lymphocytopenia

I. Tests for HIV-1

A. Virus Culture (not used in routine testing)

1. Peripheral Blood Mononuclear Cell (PBMC) Co-Culture (standard procedure): PBMCs are separated from blood of suspected HIV-infected individual, co-cultured with PBMCs from normal donor [normal PBMCs are stimulated with phytohemagglutinin (PHA)] using special culture medium (contains IL-2). Cultures observed microscopically for syncytial formation and tested for production of HIV-1 reverse transcriptase (RT) and/or p24 antigen. "Positive" = 2 assays positive for RT or p24 antigen. 95-99% of HIV-infected individuals are "positive". During the course of HIV infection at CD4 of $\sim 300/\text{mm}^3$, a change in phenotype from non-syncytium inducing (NSI) to syncytium-inducing (SI) isolates often occurs. SI isolates associated with more rapid decline in CD4 cells and disease progression.
2. Quantitative Cell Culture (used to quantify "viral load"): As in PBMC co-culture but HIV+ patient cells are diluted in 10-fold increments, i.e., 10^3 , 10^4 , 10^5 . Endpoint = reciprocal of highest dilution which is +.
3. Quantitative Plasma Culture (used to quantify "viral load"): Serial dilutions of patient's plasma are added to special culture medium; the mixture is then added to PHA-stimulated normal PBMCs. Endpoint = reciprocal of the highest dilution which is positive for p24 antigen.

B. Antibody Tests (used in standard HIV screening, except in neonates)

1. ELISA (enzyme-linked immunosorbent assay): Used to detect anti-HIV-1 antibodies in serum. A number of commercial "kits" are licensed for use. An individual's serum is added to HIV-1 antigen-coated wells in microtiter plates. The unbound serum is washed off, then goat antihuman antibody, which has been conjugated to an enzyme, is added. After washing away the unbound goat antibody, enzyme substrate is added. The bound enzyme hydrolyzes the substrate with development of a color which is read spectrophotometrically. Specificity and sensitivity can be modified by changing the optical density which defines + or -.

Saliva has been studied as an alternative to serum for HIV antibody testing with ELISA in surveillance programs in developing countries. Sensitivity is 91-100%, specificity 99.8-100%, but less than U.S. standards (*Lancet* 340:1496, 1992). Saliva tests not FDA-licensed in U.S. (June 1, 1994).

2. Western Blot: Used to detect anti-HIV antibodies but also allows determination of specific HIV antigens against which antibodies are directed. HIV-1 antigens are prepared from lysates of HIV-infected cells, separated electrophoretically on a polyacrylamide gel. Proteins (antigens) within the gel are "blotted" onto nitrocellulose filter paper. Strips of the filter paper are inoculated with test serum. HIV antibodies bind to specific antigens. The antibody bands are detected with goat antihuman antibody bound to an enzyme or by a radioactive probe.

Major antigen groups in HIV-1 are:

- Envelope (env) region: gp160, gp120, gp41 (gp = glycoprotein)
- Polymerase (pol) region: reverse transcriptase p66, p51 (p = protein) and an endonuclease, p31
- Group specific antigen (gag) region: encodes for structural proteins, p55, p24, p18

3. Rapid Screening Anti-HIV-1 Antibody Tests

- a. Latex agglutination. Uses polystyrene beads coated with HIV-1 proteins (Cambridge "Recombigen" HIV agglutination, DuPont "Hiv-Chek"). These have excellent specificity but less than optimal sensitivity (*AIDS* 3:313, 1989).
- b. Microparticle filtration tests. SUDS (Murex) and Genic (Genetic Systems) are rapid (done in ≤ 10 minutes) and accurate, but costly (U.S. \$3-12 each) (*Lancet* 340:1541, 1992).
- c. Gelatin particle agglutination. "Serodra." Good sensitivity and negative predictive value but low specificity.
- d. Autologous red cell agglutination. Uses a mouse monoclonal antibody (mAb) reagent against human RBCs. HIV-1 gp41 protein is conjugated to the mouse mAb. The mAb complex binds to patient RBCs. If gp41 antibodies are present, rapid agglutination occurs (*Science* 241:1352, 1988).

C. p24 Antigen Assays (may be of particular value in neonates)

1. p24 antigen test. Uses ELISA sandwich technique to measure p24 viral protein in plasma or tissue culture supernatant. Unfortunately, p24 antigen can only be reproducibly detected shortly following acute infection (seroconversion) and in late-stage HIV disease. p24 antigen is often undetectable when significant levels of culturable virus or viral RNA are found in the same specimen. Current tests can detect 7-10 pg/ml.
2. Immune complex-dissociated (ICD p24) or acidified p24 antigen test. Acidification (with glycine hydrochloride) disrupts antigen-antibody complexes, releasing free antigen for detection. May be useful especially in assessing neonates (*NEJM* 328:297, 1993; *J Inf Dis* 167:1193, 1993).

D. Polymerase Chain Reaction Techniques (still a research tool)

Quantitative competitive polymerase chain reaction (QC-PCR). Method developed to ↓ earlier PCR methodologic problems. Used to copy HIV RNA in plasma into a DNA form which is then amplified. Can detect HIV RNA in plasma of **all** infected individuals, as few as 50 virions/ml (*Feinberg AIDS/HIV Treatment Direct* 7:7, 1993).

- E. Branched DNA Assay (bDNA). Used to measure amount of HIV RNA in plasma. Uses highly sensitive branched DNA probes bound on an assay plate to detect RNA sequences. The bDNA probes have an enzyme attached which catalyzes release of a chemiluminescent material from its substrate. Sensitivity derives from signal amplification rather than target amplification (subject to contamination). Detection limit is 5000 virions/ml. It is less sensitive than QC-PCR but can detect and quantitate HIV RNA in ≥ 90% of HIV+ with CD4 < 500. It is faster and less expensive than QC-PCR.

II. Interpretation of HIV Antibody Tests

- A. The initial screening test to detect antibodies to HIV is the enzyme-linked immunosorbent assay (ELISA or EIA). A reactive (positive) ELISA in two sequential tests has a sensitivity of 98% and a specificity of 99.8%. But even this excellent specificity yields a low positive predictive value when testing in populations at low risk. When the prevalence is 0.3/1000 (30/100,000), 3 of 4 repeatedly positive tests will be false positive. Therefore, it is essential to perform a supplemental test to detect specific antibodies, e.g., a Western blot. If the ELISA is negative, a Western blot is usually not done.
- B. Centers for Disease Control criteria (the standard): A reactive (positive) Western blot is one which shows antibody bands against any two of the following antigens: p24, gp41, or gp120/160, (MMWR 40:681, 1991).
- C. Interpretive criteria (other than CDC)
- American Red Cross: at least one band from each gene product group: Gag and pol and env.
 - Consortium for Retrovirus Serology Standardization: p24 or p31 and one of gp41 or gp120/160.
 - DuPont: p24 and p31 and gp41 or gp120/160 (MMWR 40:692, 1991).
- (See I.B.2 for major genes and gene products of HIV)
- D. An "indeterminate" pattern (non-diagnostic) is one which reacts against only one of these antigens, usually the p24.
- E. Some "indeterminate" results may be obtained in individuals who have early infection and are in the seroconversion phase.
- F. Individuals with an indeterminate test(s) should have the Western blot repeated in 6–12 weeks and at 6 months. If a second antibody develops, the individual is positive. If negative or still "indeterminate", individuals can be reassured that they almost certainly are not infected with HIV-1.
- G. If the ELISA is repeatedly positive and the Western blot is completely negative, individuals can be reassured that they are not infected but blood bank policy still excludes them as blood donors.

III. Evaluation of Immunologic Status

- A. CD4 Cell (T-helper cell, T4 lymphocyte) Count (not a surrogate test for diagnosis of HIV infection). CD4 lymphocytes are primary targets of HIV infection.
1. Function: Respond to class II major histocompatibility complex antigens, release cytokines that activate and augment the immune response.
 2. Measurement: CD4 and CD8 cells are measured by interaction with fluorescent monoclonal antibodies and counted in fluorescent antibody cell sorting (FACS) machines. The number of CD4 cells is not determined directly but is calculated as follows: $CD4 = WBC \times \% \text{ lymphocytes} \times \% \text{ CD4 cells}$ (small variations in WBC or % lymphs greatly influence CD4 counts) [MMWR 43:(RR-3) 1–21, 1994].
 3. Variability
 - a. Individual: CD4 ↑ 15% between 8:00 a.m. and 10:00 p.m. Variations up to 200/mm³ in course of 1 day seen in 2/3 of HIV+ individuals (*J AIDS* 3:144, 1990). In 6% of asymptomatic HIV+, CD4 count was 1/2 or 2x the value obtained 8 weeks before (variation ↑ in pts with lower counts) (*J Inf Dis* 169:28, 1994).
 - b. Interlaboratory: 15–16% variation
 - c. 95% confidence limits for a single CD4 value (based on 22,322 samples from 3145 initially HIV-negative homosexual men drawn at 6-month intervals (*J AIDS* 5:794, 1992):
 CD4 800/mm³ (95% confidence limits 475–1347)
 CD4 500/mm³ (95% confidence limits 297–841)
 CD4 300/mm³ (95% confidence limits 178–505)
 - d. Intercurrent illness: CD4 counts ↓ with viral and other infections.

4. Usefulness

- a. Is the most established single test. As HIV infection advances, there is a progressive decline in CD4 cells (Table 4).
 - b. Risk of opportunistic infection increases when $CD4 < 200/mm^3$, risk of death increases when $< 50/mm^3$. But individual patients may be asymptomatic for long periods of time with $CD4 < 50/mm^3$; therefore, not a reliable predictor of prognosis in individual patient.
- B. CD4%: Not as established as CD4 count, but less variable.
 $\geq 29\% = CD4 > 500$, $14-28\% = 200-499$, $14\% = < 200$
- C. Beta-2 Microglobulin: Used to predict probability of disease progression. Is a non-specific marker of T-cell activation. Higher levels (> 3.5) correlate with progression but less specific than CD4 counts. May be $\uparrow$ with intercurrent illness. $\uparrow$ CSF levels are associated with AIDS dementia complex (Neurology 39:830, 1989).
- D. Neopterin: A marker of monocyte-macrophage activation. Higher levels (> 15 ng/ml) correlate with progression. Not established as having additional value compared to CD4 counts or %. $\uparrow$ CSF levels are associated with AIDS dementia complex (Neurology 39:830, 1989).
- E. Delayed Cutaneous Hypersensitivity (skin testing)
1. The U.S. Army (Walter Reed) natural history study has shown that for any given CD4 level, loss of skin reactivity (anergy) to standardized antigens is associated with more rapid progression. For example, with CD4 counts between 200-500, 75% survival rate with anergy was 19 months, partial reactivity 31 months, normal reactivity 43 months (J AIDS 6:1248, 1993; J Inf Dis 169:893, 1994).
 2. Intradermal skin tests performed with the following standardized antigens (J AIDS 6:1248, 1993): 0.1 ml *Candida albicans* (1:10 Dermatophyton O, Hollister-Stier); tetanus toxoid 4LF/ml (1:10 Connaught); mumps ST (40 CFU/ml, Connaught); trichophyton (1:30 Hollister-Stier) and PPD (5 TU, Connaught). Positive = ≥ 5 mm x 5 mm-induration
 - a. Normal: reactive to ≥ 2 skin test antigens
 - b. Partial defect: reactive to only 1 antigen
 - c. Anergy: reactive to none of the 4 antigens

IV. Other Human Retroviral Infections and Diagnostic Tests

A. HIV-2 (References: JAMA 267:2775, 1992; Ann Int Med 118:211, 1993; JAMA 270:2083, 1993)

1. Epidemiology. Is endemic in West Africa. Portugal and France have highest number of cases in Europe. Since 1987, 32 cases reported in U.S. (MMWR 41:RR-12, 1992). These have been sporadic without secondary spread. Spread in Africa primarily heterosexual. Heterosexual and perinatal HIV-2 transmission is less than HIV-1 with CD4 counts > 500 . In Ivory Coast, prevalence of HIV-2 has declined from 2.6 to 1.5%, while HIV-1 has $\uparrow$ from 5.0 to 9.2% (JAMA 270:2083, 1993). This low transmissibility in asymptomatic persons suggests epidemic spread may not occur and that pediatric HIV-2 may not emerge as a significant problem. HIV-2 occurs in Europe in homosexual men, injecting drug users, transfusion recipients, and men with hemophilia.
2. Recommendations for testing
 - Sex partners of a person from country where HIV-2 is endemic
 - Sex partners of a person known to be infected with HIV-2
 - Persons who received a transfusion of blood or non-sterile injection in a country where HIV-2 is endemic
 - Persons who shared needles with a person from an HIV-2 endemic country
 - Children of women who are HIV-2 infected or have risk factors
3. Test procedures
 - a. 60-91% of HIV-2 infected patients will be $\uparrow$ by HIV-1 whole lysate EIA.
 - b. FDA-licensed HIV-1/HIV-2 EIAs and FDA-licensed HIV-2 EIA $> 99\%$ sensitivity, but diagnosis requires supplemental test such as HIV-2 Western blot (none is currently licensed).
4. Blood products. Effective June 1, 1992, blood centers in U.S. began testing all donated whole blood, blood components and plasma for HIV-2 antibodies.

B. Human T-Lymphotropic Virus Type I (HTLV-I) (Reference: Ann Int Med 118:448, 1993)

1. Epidemiology. HTLV-I is endemic in southwestern Japan, the Caribbean basin, Melanesia, and in parts of Africa. Transmission is from mother to child, by sexual contact, by blood transfusion (up to 20% recipients will develop tropical spastic paraparesis after transfusion of HTLV-1 + blood), and by sharing contaminated needles. HTLV-I is not transmitted by casual contact.

2. Clinical. Two diseases have been associated with HTLV-I.
 - a. Adult T-cell leukemia/lymphoma
 - b. HTLV-I associated myelopathy/tropical spastic paraparesis
3. Testing. In Nov. 1988, FDA issued recommendations to screen all whole blood and blood component donations in U.S. for HTLV-I. Seroprevalence rates among donors average 0.016%. In 1991, an association between recent (mean 26 days) influenza virus vaccination (IVV) and false-positive ELISA tests for HIV, HTLV-I and hepatitis C virus (HCV) was reported in 0.6-1.7% of vaccinated blood donors (*JAMA* 268:1015, 1992). This was attributed to non-specific IgM cross-reactivity. In early 1992 new kits for HIV and HCV reduced or eliminated this problem, but an estimated 1.7-4.9% of blood donors immunized with IVV still had false + ELISAs for HTLV-I. Fortunately, the duration of false + reactivity is ≤ 4 months (*MMWR* 42:173, 1993).
4. Counseling. Seropositive persons should be informed that they are infected with HTLV-I. It is not the AIDS virus. They should be advised that it is a life-long infection; they should not donate blood or organs, not share needles, not breast-feed infants, and consider the use of latex condoms to prevent sexual transmission.

C. Human T-Lymphocytotropic Virus Type II (HTLV-II) (Reference: *Ann Int Med* 118:448, 1993)

1. Epidemiology. Endemic in American Indian populations. Also prevalent in injecting drug users in the U.S. and Europe. Over 80% of HTLV-I/II seropositivity in IDUs is due to HTLV-II (*NEJM* 326:375, 1992). Transmission is assumed similar to HTLV-I.
2. Clinical. Has not been clearly associated with any diseases, although two women reported with olivopontocerebellar atrophy (*Lancet* 339:645, 1992).
3. Testing. As of March 25, 1993, a decision for screening blood donors for HTLV-II was deferred [low prevalence estimated at 1:10,000, risk of acquisition $\sim 30\%$, vague nature of disease reports (*Lancet* 341:888, 1993)].

V. Idiopathic CD4 T-Lymphocytopenia (*NEJM* 328:429, 1993)

- There is a syndrome of idiopathic CD4 T-lymphocytopenia in people (a few of whom have had opportunistic infections) who are seronegative for HIV-1, HIV-2, HTLV-I, HTLV-II, and in whom no other obvious causes of immunosuppression can be identified.
- Persistently low ($< 300/\text{mm}^3$) CD4 counts are rare, less than 1/10,000 person years of observation (*NEJM* 328:442, 1993).
- Cases have been identified as early as 1983.
- Less than $\frac{1}{2}$ patients had risk factors for HIV. $\frac{1}{2}$ were women. CD4 lymphocytopenia remained stable over time. Immunoglobulin levels normal or $\downarrow$ in contrast to HIV-infected patients, in whom Ig levels are $\uparrow$.
- Virologic studies are negative and there is no epidemiologic evidence to suggest a transmissible agent.

TABLE 3A
1993 REVISED CDC HIV CLASSIFICATION SYSTEM AND EXPANDED AIDS SURVEILLANCE DEFINITION FOR ADOLESCENTS AND ADULTS
(MMWR 41:RR-17, Dec. 18, 1992)

The revised system emphasizes the importance of CD4 lymphocyte testing in clinical management of HIV infected persons. The system is based on 3 ranges of CD4 counts and 3 clinical categories giving a matrix of 9 exclusive categories. The system replaces the 1986 classification.

CRITERIA FOR HIV INFECTION: Persons 13 years or older with repeatedly (2 or more) reactive screening tests (ELISA) + specific antibodies identified by a supplemental test, e.g., Western blot ["reactive" pattern = + vs any two of p24, gp41, or gp120/160 (MMWR 40:681, 1991)]. Other specific methods of diagnosis of HIV-1 include virus isolation, antigen detection, and detection of HIV genetic material by PCR.

CLASSIFICATION SYSTEM				Clinical Category A	Clinical Category B	Clinical Category C
CD4 Cell§ Category	CLINICAL CATEGORY			Asymptomatic HIV infection Persistent generalized lymphadenopathy (PGL) ¹ Acute (primary) HIV illness	Symptomatic, not A or C conditions. Examples include but not limited to: Bacillary angiomatosis Candidiasis, vulvovaginal: persistent > 1 month, poorly responsive to rx Candidiasis, oropharyngeal Cervical dysplasia, severe, or carcinoma in situ Constitutional sx, e.g., fever (38.5°) or diarrhea > 1 month	Candidiasis: esophageal, trachea, bronchi Coccidioidomycosis, extrapulmonary Cryptococcosis, extrapulmonary † Cervical cancer, invasive Cryptosporidiosis, chronic intestinal (> 1 month) CMV retinitis, or CMV in other than liver, spleen, nodes HIV encephalopathy Herpes simplex with mucocutaneous ulcer > 1 month, bronchitis, pneumonia Histoplasmosis: disseminated, extrapulmonary Isosporiasis, chronic, > 1 month Kaposi's sarcoma Lymphoma: Burkitt's, immunoblastic, primary in brain M. avium or M. kansasii, extrapulmonary M. tuberculosis, †pulmonary or extrapulmonary Pneumocystis carinii pneumonia † Pneumonia, recurrent (≥ 2 episodes in 1 year) Progressive multifocal leukoencephalopathy Salmonella bacteremia, recurrent Toxoplasmosis, cerebral Wasting syndrome due to HIV
	A	B	C			
	(1) ≥ 500/mm ³	A1	B1	C1		
	(2) 200–499/mm ³	A2	B2	C2		
	(3) < 200/mm ³	A3	B3	C3		
* See table for clinical definitions. Shaded area indicates expansion of AIDS surveillance definition. Cat. C currently "reportable", Cats. A3 and B3 are "reportable" as AIDS effective January 1, 1993. § There is a diurnal variation in CD4 counts averaging 60/mm³ higher in the afternoon in HIV+ individuals and 500/mm³ in HIV– persons. Blood for sequential CD4 counts should be drawn at about the same time of day each time (<i>J AIDS</i> 3:144, 1990). The equivalence between CD4 counts and CD4 % of total lymphocytes is ≥500 = ≥29%, 200–499 = 14–28%, <200 = <14%.				The above must be attributed to HIV infection or have a clinical course or management complicated by HIV.		
				¹ Nodes in 2 or more extralingual sites, at least 1 cm in diameter for ≥ 3 months	* These are the 1987 CDC case definitions (MMWR 36:15, 1987). The 1993 CDC Expanded Surveillance Case Definition includes all conditions contained in the 1987 definition (above) plus persons with documented HIV infection and any of the following: (1) CD4 T-lymphocyte count < 200/mm³ (or CD4 < 14%), (2) pulmonary tuberculosis,† (3) recurrent pneumonia† (≥ 2 episodes within 1 year) or (4) invasive cervical carcinoma.†	

TABLE 3B
WALTER REED STAGING CLASSIFICATION FOR HIV INFECTION

STAGE	HIV ANTIBODY OR ANTIGEN OR VIRUS ISOLATION	CHRONIC LYMPHADENO- PATHY ⁽¹⁾	CD4 CELLS/mm ³ ⁽²⁾	DELAYED CUTANEOUS HYPERSENSITIVITY ⁽³⁾	THRUSH ⁽⁴⁾	OPPORTUNISTIC INFECTIONS ⁽⁵⁾
WR 0	—	Possible or probable exposure				
WR 1	+	0	> 400	normal	0	0
WR 2	+	+	> 400	normal	0	0
WR 3	+	±	< 400*	normal	0	0
WR 4	+	±	< 400	partial loss*	0	0
WR 5	+	±	< 400	complete and/or	+	0
WR 6	+	±	< 400	partial or complete	±	+

* Essential criteria for assignment to stage: (1) Nodes in 2 or more extrainguinal sites, at least 1 cm diameter for ≥ 3 months. (2) Decreased for ≥ 3 months. (3) Induration ≥ 5 mm to at least 2 of the following test antigens: tetanus, trichophyton, mumps, candida (See Table 2, page 8 for details). (4) Thrush = clinical oral candidiasis with + KOH or Gram stain. (5) Opportunistic infections include those in 1987 CDC case definition Clinical Category C, Table 3A.

—Reproduced with permission from New Eng J Med 314:132, 1986

TABLE 3C
'PERFORMANCE STATUS' (KARNOFSKY SCALE)

Criteria of Performance Status (PS)		
Able to carry on normal activity; no special care is needed	100	Normal; no complaints; no evidence of disease
	90	Able to carry on normal activity; minor signs or symptoms of disease
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; a varying amount of assistance is needed	70	Cares for self; unable to carry on normal activity or to do active work
	60	Requires occasional assistance but is able to care for most needs
	50	Requires considerable assistance and frequent medical care
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly	40	Disabled; requires special care and assistance
	30	Severely disabled; hospitalization is indicated although death not imminent
	20	Very sick; hospitalization necessary; active supportive treatment is necessary
	10	Moribund, fatal processes progressing rapidly
	0	Dead

TABLE 4
COURSE OF HIV INFECTION AND DISEASE IN ADULTS: CLINICAL DECISION POINTS

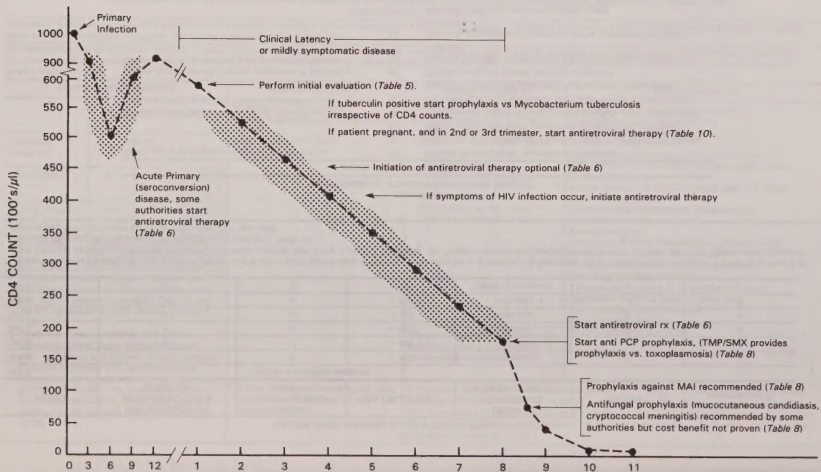


TABLE 4A
MAJOR AIDS CLINICAL TRIALS*

PROTOCOL NUMBER	TITLE AND SUMMARY OF CLINICAL TRIAL	REFERENCE
Burroughs-Wellcome 02	Zidovudine versus placebo in patients with previous diagnosis of <i>P. carinii</i> pneumonia. Zidovudine dosage 1500 mg/d. Showed significant ↓ in mortality and ↓ in opportunistic infections (PCP). Pts not on anti-PCP prophylaxis.	NEJM 317:185, 1987
ACTG 002	Multicenter clinical trial to evaluate efficacy and safety of lower dose ZDV in treatment of HIV infection in patients with AIDS post first episode PCP. 250 mg q4h (1500 mg qd) vs 100 mg q4h (600 mg qd). No difference in efficacy, considerably less toxicity with 600 mg qd.	NEJM 323:1009, 1990
ACTG 016	Safety and efficacy of ZDV in treatment of patients with mildly symptomatic disease. CD4 < 500 but > 200/mm ³ and > 500- < 800. Placebo vs zidovudine 200 mg q4h (1200 mg/d). In pts with < 500 CD4/mm ³ , ZDU delayed progression, ↑ CD4 with little toxicity.	Ann Int Med 112:727, 1990
ACTG 019	Safety and efficacy of ZDV (higher and lower doses) vs placebo in asymptomatic patients. CD4 > 500 and CD4 < 500. Zidovudine 300 mg 5x/d (1500 mg/d) vs 100 mg 5x/d (500 mg qd). Significant ↓ in progression (especially 500 mg qd)—mostly delay in occurrence of PCP. Mean study period 55 weeks. 016 and 019 led to FDA approval of zidovudine 500 mg qd for pts with < 500 CD4.	NEJM 322:941, 1990
VA Cooperative Study 298	Compared immediate zidovudine (1500 mg/d) vs deferred zidovudine in mildly symptomatic patients with CD4 < 500- > 200/mm ³ . In deferred group, zidovudine started when CD4 < 200/mm ³ or AIDS. Immediate rx significantly delayed progression but had more side-effects and did not ↑ survival after an average study period of 2 years, but confidence interval 0.6-1.8.	NEJM 326:437, 1992
Concorde I Trial	Efficacy of zidovudine vs placebo in asymptomatic patients, endpoints of death or progression to AIDS (British-French trial). CD4 < 500. Zidovudine 250 mg 4x/d (1000 mg qd). 3-year study interval. No difference in progression or survival, although rate of progression ↓ in first 55 weeks (similar to 019).	Lancet 343:871, 1994
European-Australian Collaborative Group Protocol 020	Efficacy of zidovudine (500 mg 2x/d) vs placebo in asymptomatic patients with CD4 > 400/mm ³ . Study showed 40-50% ↓ in progression to CDC Group IV or ↓ in CD4 to < 350/mm ³ but no ↓ in progression to AIDS after 2 years. Rx well tolerated (22% required dose modification).	NEJM 329:297, 1993
Burroughs-Wellcome 017	Efficacy of zidovudine vs placebo in asymptomatic patients, CD4 > 200- < 400/mm ³ (European-Australian). No ↓ in progression to AIDS or severe ARC after 2 years. However, rate of progression in 1st year was higher on placebo. Similar to 019, Concorde I.	Cited in JAMA 270:2583, 1993
ACTG 116A	Comparison of didanosine (ddi) and zidovudine in therapy of patients with HIV infection who had received none or < 16 weeks zidovudine. Didanosine (500 mg and 750 mg qd) vs zidovudine (600 mg qd), pts with advanced HIV. No difference in progression to AIDS or death, although trend favored 500 mg didanosine. Didanosine and zidovudine appear equivalent in efficacy.	Cited in JAMA 270:2583, 1993
ACTG 116B/117	Comparison of didanosine and zidovudine in pts with HIV infection who have been on long-term zidovudine. Pts on zidovudine > 16 weeks (median 13.9 months), symptomatic with CD4 < 300/mm ³ or asymptomatic with < 200/mm ³ . Zidovudine 600 mg qd, didanosine 500 mg or 750 mg/d. Changing rx from zidovudine to ddi 500 mg/d significantly ↓ progression.	NEJM 327:581, 1992

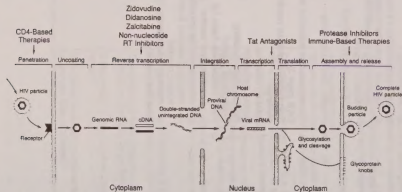
* Investigators often discuss recommendations based on protocol numbers, which are jargon to most. This is a summary of those trials, results and references. They are the basis for current recommendations.

PROTOCOL NUMBER	TITLE AND SUMMARY OF CLINICAL TRIAL	REFERENCE
Bristol-Myers Squibb 454-010	Didanosine 600 mg/d compared with continuation of zidovudine (800 mg/d) in pts with signs of clinical deterioration on zidovudine. 76% > 12 months zidovudine. 60% CD4 < 100/mm ³ . Signs of deterioration: weight loss 22%, thrush or oral hairy leukoplakia 50%, skin disease 25%, CD4 ↓ 36%. Pts switching from zidovudine to ddI showed less progression (especially if CD4 > 100/mm ³).	Ann Int Med 120:360, 1994
CPCRA Protocol 002	Comparison of didanosine (500 mg/d) or zalcitabine (2.25 mg/d) in patients who failed or were intolerant of zidovudine. Most pts had been on zidovudine 500-600 mg/d, x17 months, CD4 median 37/mm ³ . Median follow-up 16 months, 157/230 ddI died vs 152/237 ddC. When stratified by Karnofsky score and CD4, ddC more effective than ddI vs survival, not disease progression. Conclusion: ddI and ddC of equal efficacy in pts who are intolerant or progressing while on zidovudine.	NEJM 330:657, 1994
ACTG 155	Comparison of zalcitabine alone vs zalcitabine + zidovudine in pts on prior zidovudine. No benefit in empirically switching from zidovudine to ddC or to adding ddC (combined rx) if pt not intolerant or deteriorating on zidovudine.	Cited in JAMA 270:2583, 1993
European Alpha Trial	200 mg/d of didanosine in sachet form is as effective on disease progression but with less toxicity than 750 mg/d.	Lancet 340:1346, 1992
ACTG 152	Comparison of zidovudine vs didanosine vs ZDU + ddI in symptomatic children	Not completed
ACTG 076	Efficacy of zidovudine for prevention of maternal-fetal transmission of HIV. See Table 10	MMWR 43:185, 1994 (April 24)
ACTG 159	Comparison of amphotericin B + flucytosine vs amphotericin B alone followed by comparison of fluconazole vs itraconazole suppression in cryptococcal meningitis	Not completed
ACTG 175	Evaluation of monotherapy vs combination therapy with nucleoside analogues in pts with CD4 < 500-→ 200/mm ³ but recently modified to look at early vs deferred combination rx	Not completed
ACTG 196	Evaluation of clarithromycin vs rifabutin vs combination clarithromycin + rifabutin in prevention of MAC in pts with CD4 < 100/mm ³	Not completed
ACTG 241	Comparison of a combination of zidovudine + didanosine + nevirapine vs zidovudine + didanosine	Not completed
ACTG 981	Comparison of fluconazole vs clotrimazole troches in prevention of serious fungal infections in patients with AIDS	Not published
CP 007	Comparison of zidovudine vs zidovudine + ddI vs zidovudine vs ddC	Not completed
CP 009	Comparison of clarithromycin vs placebo in prevention of MAC in pts with CD4 < 100/mm ³	Not published

INITIAL EVALUATION OF THE HIV-INFECTED ADULT PATIENT (JAMA 269:1144, 1993)

- | | |
|---|---|
| <p>I. History</p> <p>A. General health status</p> <ol style="list-style-type: none"> 1. General well-being 2. Constitutional symptoms 3. History of infectious diseases: childhood infections, infections in adult life, previous physician visits, hospitalizations (where, when) 4. Immunization history <p>B. Drug history</p> <ol style="list-style-type: none"> 1. Medications <ol style="list-style-type: none"> A. Prescription B. Non-prescription C. Alternative therapies, e.g., compound Q (see Table 21) 2. Recreational drug use (See Table 1, page 3) <ol style="list-style-type: none"> A. Intravenous/injection B. Other C. Partners at risk 3. Smoking history 4. Alcohol history <p>C. Sexual history</p> <ol style="list-style-type: none"> 1. Sexual practices (See Table 1, page 3) 2. Sexually transmitted diseases 3. Obstetrical/gynecologic history 4. Contraceptive use 5. Partners at risk <p>D. Risks for opportunistic infections</p> <ol style="list-style-type: none"> 1. Travel history 2. Geographic location of current/prior residence, e.g., southwestern, mideastern USA 3. Occupational history, e.g., poultry workers 4. Avocational activities 5. Tuberculosis status: history of BCG vaccination, family members with and/or treated for tuberculosis, contacts (close) with patients with known tuberculosis, results of previous tuberculin tests and/or chest x-rays if known 6. Pets, e.g., cats—<i>Bartonella</i> (Rochalimaea) henselae; fish—<i>M. marinum</i>. Cat ownership not associated with toxoplasma antibody seroconversion (JAMA 269:76, 1993) <p>E. Past history of viral hepatitis, to include type if known</p> | <p>III. Laboratory Evaluation</p> <p>A. Baseline</p> <ol style="list-style-type: none"> 1. Complete blood count with differential 2. Renal function tests: BUN, creatinine 3. Liver function tests: serum bilirubin, aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), alkaline phosphatase <p>B. HIV staging</p> <ol style="list-style-type: none"> 1. CD4 count/percent CD4 cells 2. ESR (optional) <p>C. Additional studies</p> <ol style="list-style-type: none"> 1. PPD intermediate (5TU) with controls 2. Chest x-ray 3. VDRL or RPR 4. Anti-toxo IgG 5. HBV sAg/sAb/cAb, if indicated 6. Delayed cutaneous hypersensitivity (skin) testing (optional but useful, see Table 2, page 8) 7. HCV antibody (optional) <p>IV. Initial Health Care Maintenance</p> <p>A. HIV risk reduction education (see Table 1, II.A,B, page 3)</p> <p>B. Drug rehabilitation/safer needle use/needle exchange</p> <p>C. Smoking cessation</p> <p>D. Partner notification</p> <p>E. Reproductive counseling</p> <p>F. Psychosocial support</p> <p>G. Immunizations (see Table 13)</p> <ol style="list-style-type: none"> 1. Pneumococcal vaccine 2. Influenza vaccine (annually) 3. Hepatitis B vaccine, if sexually active or sharing needles 4. Haemophilus influenzae type b vaccine <p>H. Preventive dentistry</p> |
|---|---|
- II. Comprehensive Physical Examination
- A. Document weight and height
 - B. Careful funduscopic and oral examination
 - C. Dermatologic examination, to include back and extremities, hands, feet
 - D. Exam of all lymph node areas: postoccipital, preauricular, cervical, submental, supraclavicular, axillary, epitrochlear, inguinal (measure and record size if palpable, record as negative if not palpable)
 - E. Rectal/genital examination, to include pelvic exam with Pap smear in women, inspection for perianal/genital Herpes simplex. Pap smears should be repeated every 12 months.

TABLE 6A
TREATMENT WITH ANTIRETROVIRAL DRUGS
REPLICATIVE CYCLE OF HIV-1, SHOWING SITES OF ACTION OF ANTIVIRAL AGENTS*



* Reproduced with permission
 from Hirsch MS, D'Aquila RT,
NEJM 328:1686, 1993 (June 10)

ANTIRETROVIRAL (HIV-1) THERAPY FOR ADULTS* (FDA-approved drugs, June 1, 1994)

NO PREVIOUS ANTIRETROVIRAL THERAPY			PREVIOUS ANTIRETROVIRAL THERAPY			INTOLERANT TO ZIDOVUDINE		
CLINICAL STATUS	CD4 CELL COUNT, RANGE (/mm ³)	RECOMMENDATION	CLINICAL STATUS	CD4 CELL COUNT, RANGE (/mm ³)	RECOMMENDATION	CLINICAL STATUS	CD4 CELL COUNT, RANGE (/mm ³)	RECOMMENDATION
Asymptomatic	> 500	No therapy	Stable	≥ 300	Continue zidovudine	Stable or progressing	< 500	Change to didanosine or zalcitabine
Asymptomatic	200-500	Zidovudine** or no therapy	Stable	< 300	Continue zidovudine or change to didanosine			
Symptomatic	200-500	Zidovudine**	Progressing	50-500	Change to didanosine or zalcitabine			
Asymptomatic	< 200	Zidovudine	Progressing	< 50	Change to didanosine or zalcitabine			
Symptomatic	< 200	Zidovudine						

* Adapted with permission from *JAMA*, Dec. 1, 1993, 270:2583-2589, copyright 1993. These recommendations represent a consensus. There are a number of experienced AIDS investigator/clinicians who disagree with some of the recommendations, e.g., no previous antiretroviral rx, asymptomatic, CD4 200-500; they do not believe "no therapy" is appropriate. Decisions regarding therapy should involve patient understanding and input regarding treatment options. ** Although not supported by clinical trials, some physicians choose to treat with combined therapy (ZDU, ddI, ddC); however, toxicity may ↓ quality of life without ↑ survival.

TABLE 6A (2)

ANTIRETROVIRAL DRUGS FOR TREATMENT OF ADULTS: DOSAGE, ROUTE, COST*, ADVERSE EFFECTS, AND COMMENTS

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE/COST	COMMENTS/ADVERSE EFFECTS
Food and Drug Administration Approved Reverse transcriptase inhibitors:		
Zidovudine formerly azido- thymidine (ZDV) (Retrovir)	po or IV q8h 100 mg cap (po) \$1.49 200 mg IV \$160.99	Zidovudine (ZDV) is approved (indicated) for adult patients with HIV infection with CD4 < 500/mm ³ . Also for children > 3 months who have HIV-related symptoms or have lab values indicating immunosuppression. A randomized multicenter double-blind clinical trial of zidovudine to prevent HIV transmission from mothers to their infants (ACTG 076) has shown (within the limits of the study) a decrease in transmission from 25.5% on placebo to 8.3% on ZDV (p < 0.001). The PHS has made interim recommendations (MMWR 43:265, 1994 (April 25)) although current FDA-approved labeling does not include this indication. For details, see Table 10. Adverse effects: Most are dose-dependent. On 600 mg/d: Major clinical toxicity is hematologic: anemia (< 8 gm, 1%), granulocytopenia (< 750, 1.8%). Macrocytosis expected with all dosage regimens. Anemia may respond to epoetin alfa if endogenous serum erythropoietin levels are ≤ 500 mU/ml. Other: GI—nausea 50%, xerostomia, hypertriglyceridemia, hepatomegaly with severe steatosis and severe lactic acid acidosis (AIDS Clin Care 6:17, 1994), anorexia 20%, vomiting 17%, CNS—headache 62%, malaise 53% (headache, malaise at initiation of rx less frequent if dose 200 mg qd for 5–7 days, then 400 mg q12h for 5–7 days, then 200 mg q8h); pigmentation of nails, cardiomyopathy (v. rare), myopathy (7/41 pts on ZDV > 270 days, creatine kinase ↑ 2 months before clinical signs, biopsies show abnormal giant mitochondria, strength returns ~ 8 weeks after ZDV discontinued, <i>Quart J Med</i> 86:5, 1993); leukocytoclastic vasculitis. Resistance of HIV to ZDV, especially in patients with late-stage disease on prolonged therapy (> 2 years), is common. The clinical significance is still uncertain, see Table 6Bx for more detailed review.
Dideoxynosine ddl (Didanosine) (Videx)	≥ 60 kg Tablets 200 mg q12h on empty stomach Powder 250 mg q12h on empty stomach < 60 kg Tablets 125 mg q12h on empty stomach Powder 167 mg q12h on empty stomach	Didanosine (monotherapy) is approved (indicated) for adults with advanced HIV infection who have received prolonged zidovudine therapy (pts had mean CD4 95/mm ³ and had been rx with ZDV for a median of 14 months). Also indicated for treatment of adult and pediatric patients (> 6 months) with advanced HIV infection who have intolerance to or significant clinical deterioration on ZDV. ZDV should be initial rx unless contraindicated. Pts on ddl 500 mg/d (powder) had fewer AIDS-defining events than pts continued on ZDV 600 mg/d (<i>NEJM</i> 327:581, 1992). In pts who had not taken ZDV before, ddl was less effective than ZDV (<i>Lancet</i> 341:109, 1993). Adverse effects: Pancreatitis 6% (0.35% fatal), ↑ amylase 10%, ↑ amylase can be of salivary origin esp. with xerostomia (1/3). No intervention necessary unless symptomatic. In pts with history of pancreatitis 8/27 (30%) developed pancreatitis, avoid or use with caution in alcoholics. Hyperglycemia, occasional diabetes mellitus. Peripheral neuropathy 20%, 12% required dose reduction. Hepatic: ↑ SGOT 13%, fatal liver failure in 0.2%, hepatomegaly with severe steatosis, hypertriglyceridemia. Other: GI—diarrhea 28%, abdominal pain 10%, nausea 6%, skin—rash 9% (1 case Stevens Johnson syndrome); CNS—headache 7%; fever 12%. Lab: anemia (< 8.0 gm, 2%), leucopenia (< 2000, 16%), thrombocytopenia (< 50,000, 2%), ↑ uric acid 2%. Pregnancy—use only if clearly needed. Approved for children, see Table 12E, page 90. Pts with phenylketonuria: chewable tablets contain phenylalanine 45–67 mg/dose. Pts on Na ⁺ restriction, buffered tablets each contain 265 mg Na ⁺ . Note: Drugs whose absorption can be affected by gastric acidity or buffers, e.g., dapsone, ketoconazole, fluoroquinolones, should be given 2 hours apart from ddl.
	po. Tablets (25, 50, 100, 150 mg) must be chewed or crushed thoroughly before swallowing. Buffered powder for oral solution (100, 167, 250 mg packets) to be dissolved in 4 oz water is available. (100 mg tablet \$1.44, 250 mg powder \$3.60)	

* From 1994 Red Book, Medical Economics Data. Price is average wholesale price (AWP)

TABLE 6A (3)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE/COST	COMMENTS/ADVERSE EFFECTS
Dideoxycytidine ddC, zalcitabine (HIVID)	0.75 mg q8h (dosage not ↓ if weight > 30 kg) Higher doses too toxic. po (0.75 mg tablet \$2.14)	In Sept. 1993, FDA Advisory Committee recommended ddC be approved as monotherapy in patients who have failed or are intolerant of ZDV (based on a comparison of ddl or ddC, <i>NEJM</i> 330:657, 1994). The Committee also recommended that the approval for ddC in combination with ZDV in adults with CD4 < 300/mm³ who have had significant clinical or immunological deterioration be revoked, since a large randomized trial (ACTG 155) showed no differences between ZDV, ddC and ZDV/ddC (<i>Ann Int Med</i> 118:762, 1993), although in pts with CD4 > 150/mm³ ZDV/ddC may have been more effective. Adverse effects: Major clinical toxicity is peripheral neuropathy (17-31%) (numbness and paresthesias → severe continuous pain, slowly reversible when ddC discontinued). Pancreatitis: < 1% except in pts with prior pancreatitis (3.2% pancreatitis or ↑ amylase) but fatal pancreatitis has occurred. Other: GI—oral ulcers 13%, dysphagia 3%, abdominal pain 3%; skin—rash 8%; CNS—headache 9%, myalgia 5%. Hepatomegaly with severe steatosis. Lab: Anemia 5%, leucopenia (< 1500, 9%), eosinophilia (> 25%, 2%), thrombocytopenia (< 50,000, 4%), SGOT (> 250, 5%). Dose is 0.375 mg q8h for pts with resolving ddC neuropathy. Fertile women should not receive ddC unless on effective contraception. Safety in children < 13 yrs not established.
Investigational Drugs (available through expanded access or in larger clinical trials)		
d4T, stavudine (Zerit)	30-40 mg bid po	Adverse effects: Peripheral neuropathy (20/100 pt years). GI: nausea/vomiting, abdominal pain, diarrhea, pancreatitis (4/100 pt years). CNS: sleep disorders, mania. Skin: rash. Hepatic: ↑ SGPT. Comment: Available through "expanded access" to pts intolerant of or failing on ZDV and ddl (11,000 pts enrolled). On 5/20/94, FDA Advisory Committee "supportive of approval". Manufacturer: Bristol-Myers Squibb [(212) 546-4000].
3TC, lamivudine	12 mg/kg/day po	Adverse effects: Skin: rash. CNS: insomnia, headache. GI: diarrhea. Other: vasculitis, photophobia, paresthesias in arms. No lab toxicity at < 20 mg/kg/d. At 20 mg/kg/d, neutropenia. Comment: Available through "compassionate use protocol" to pts who are refractory to or unable to tolerate approved therapies. Used as mono- or combined therapy. Manufacturer: Glaxo Inc. [(919) 941-4841].
Nevirapine (a non-nucleoside RT inhibitor)	400 mg/day po	Adverse effects: 11/32 pts discontinued because of adverse effects (starting at 200 mg/d x2 weeks appears to improve tolerance). Rash (8/32), fever, thrombocytopenia. 1 case angioedema. Comment: Rapid emergence of resistance has been a problem. Being studied in combination regimens, which appear not to ↓ resistance. Manufacturer: Boehringer Ingelheim Corp. [(203) 798-4700]
Ro 31-8959, saquinavir	600 mg tid po	Adverse effects: Headache, GI disturbances. Comments: Being studied as mono- or combined therapy. Manufacturer: Hoffman-La Roche Inc. [(201) 235-6328].

TABLE 6B
RESISTANCE OF HIV TO ANTIRETROVIRAL AGENTS

- Drug-resistant mutants of herpes simplex virus, varicella-zoster virus, cytomegalovirus, and influenza virus A have emerged under the selective pressure of chemotherapy.
- Zidovudine was licensed for general use in 1987. In 1989 decreased susceptibility, some at high level, was reported. Amino acid sequencing of the reverse transcriptase gene from "resistant" HIV isolates has shown amino acid mutations at 5 codons (41, 67, 70, 215, 219) are associated with resistance to ZDV, mutations at 74, 184 with resistance to ddI, and at 69 with resistance to ddC.
- On ZDV, in patients with late-stage disease ($CD4 < 200/mm^3$ and HIV-related symptoms) at 2 years ~ 80% had isolates with high-level resistance. With $CD4 > 200/mm^3$, high-level resistance was not seen at 2 years but was in 3rd and 4th years of ZDV rx.
- High-level ZDV resistance is associated with some ↓ susceptibility to ddI and ddC.
- ZDV "resistant" mutants have been transmitted and have been isolated from CSF.
- ZDV "resistant" mutants persist 5–22 months after ZDV is discontinued.
- Combination therapy with ZDV and ddC did not prevent emergence of ZDV "resistance".
- Disease progression seems more clearly related to the emergence of the syncytium-inducing phenotypes of HIV than to ZDV resistance.
- The clinical significance of decreased susceptibility remains unclear. Some studies, especially in children, suggest an association with disease progression and decrease in $CD4$ counts.
- The strongest evidence for an association between resistance and loss of antiviral activity comes from studies of non-nucleoside reverse transcriptase inhibitors L697661 and nevirapine.
- At present, there is no clinically available assay for detection of resistance.
- Based upon present knowledge, the consensus is that current recommendations for treatment should not be modified on the basis of isolation of a resistant strain of HIV but should be based upon the patient's clinical course.

TABLE 6C
DRUGS USED IN TREATMENT OF ANEMIA AND GRANULOCYTOPENIA: HIV AND/OR DRUG-RELATED

DRUG NAME, GENERIC (TRADE)	ADVERSE EFFECTS/COMMENTS	COST*
Recombinant erythropoietin, epoetin alfa (Epogen, Procrit)	Response observed in pts with endogenous erythropoietin levels ≤ 500 mU/ml, those with levels > 500 mU/ml did not show ↓ transfusion requirements (NEJM 322:1488, 1990). Adverse effects are common but generally tolerated. In double-blind studies in HIV + pts, differences between drug and placebo groups were not statistically significant): Fever 38%, fatigue 25%, headache 19%, cough 18%, diarrhea 16%, rash 16%, nausea 15%, shortness of breath 14%, dizziness 9%. Two ZDV-treated pts had urticarial reactions within 48 hrs of first exposure to erythropoietin. CNS: seizures (10 pts on ZDV had seizures, probably related to underlying disease rather than drug). In pts with renal failure, EPO has been associated with accelerated hypertension and thrombosis (v. rare).	4000 units \$48.00
Granulocyte colony stimulating factor (G-CSF), Filgrastim (Neupogen)	Adverse effects (clinical trials have involved primarily patients receiving cytotoxic chemotherapy, most adverse effects were sequelae of chemotherapy): Bone pain (transient) very common. Nausea and vomiting 57%, alopecia 18%, diarrhea 14%, fever 12%, fatigue 11%, anorexia 9%, dyspnea 9%, headache 7%, skin rash 6%, moderate hypotension 4%. Lab: ↑ uric acid, LDH, alkaline phosphatase in 27–55% (reversible). May activate viral expression and could accelerate course of HIV infection—patient should be on antiretroviral therapy. Sweet syndrome (acute febrile neutrophilic dermatosis) reported after G-CSF (Ann Int Med 116:996, 1992).	300 mcg \$141.00
Granulocyte-monocyte colony stimulating factor (GM-CSF), Sargramostim (Leukine)	Adverse effects (clinical trials have involved primarily patients undergoing bone marrow transplantation for non-Hodgkin's lymphoma, acute lymphoblastic leukemia, Hodgkin's disease): Bone pain (transient) very common. Diarrhea 89%, asthenia 66%, rash 44%, malaise 57% were only adverse effects observed for 5% more subjects than placebo. Lab: ↑ creatinine, bilirubin, hepatic enzymes. May activate viral expression and could accelerate course of HIV infection—patient should be on antiretroviral therapy. Comment: Most side effects prevented or reversed with antipyretics and analgesics such as acetaminophen.	250 mcg \$106.25

* From 1994 Red Book, Medical Economics Data. Price is average wholesale price (AWP)

TABLE 6D
ANABOLIC AGENTS FOR WASTING/WEIGHT LOSS (See Table 7A, page 52)

Dronabinol (Marinol): FDA-approved as an appetite stimulant in AIDS patients with wasting. It is delta-9-THC, a major active substance in marijuana, a narcotic Schedule II controlled substance. Patients on 2.5 mg po bid have significant ↑ in appetite and weight gain over patients on placebo. **Adverse effects:** CNS: dose-related "high" (euphoria, easy laughing) 8%, dizziness, confusion, paranoid reaction, somnolence (3-10%). GI: nausea, vomiting (2.5 mg cap \$2.99)

Megestrol acetate (Megace): A synthetic oral progesterone approved for anorexia, cachexia or unexplained significant weight loss in AIDS patients. 800 mg po qd ↑ appetite and sense of well-being. 64% patients gained ≥ 5 lbs (VII Int Conf AIDS, Florence, 2-290, 1991). **Usual dose** is 800 mg po qd x1 month, then 400 mg po qd x4 months. **Adverse effects:** diarrhea, rash, impotence, edema, flatulence, weakness. (8 oz, 40 mg/ml, \$103.80 = \$8.65/800 mg)

Fluoxymesterone (Halolestin): Approved as an androgen replacement in men and for recurrent breast carcinoma in women. Placebo-controlled trial in progress (10 mg po bid) in AIDS wasting syndrome. (10 mg tab \$1.38)

Recombinant Human Growth Hormone (rHGH) (Protropin): rHGH is approved for treatment of children with endogenous growth hormone deficiency. rHGH (2.5-5.0 mg SC 3x weekly) + insulin-like growth factor I (IGF-I) in Phase II clinical trial. (5.0 mg \$210.00)

Fat Emulsions, intravenous: A Phase II open label clinical trial with Liposyn III in progress.



TABLE 7A*

EVALUATION OF CLINICAL SYNDROMES, OPPORTUNISTIC INFECTIONS, NEOPLASMS, AND DIFFERENTIAL DIAGNOSES

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS												
Central Nervous System (includes myelopathy, neuropathy, meningitis) [Useful diagnostic tests: Neurological exam, CT scan or MRI (T1 and T2 weighted images, gadolinium infusion), CSF exam (pressure, cells, protein, glucose, CRAG, Gram stain, India ink prep, culture [bacteria, AFB, fungi], syphilis serology [VDRL], cytospin for malignant cells, serum [toxoplasma antibodies, CRAG])														
Cognitive Disorders Declining mental status: difficulty in memory, concentration, mathematical calculations	HIV-associated minor cognitive dysfunction (<i>Neural</i> 41:778, 1991), also known as AIDS dementia complex: AIDS dementia complex (Price & Worley, 1994)** Stage 0: normal Stage 1: mild, can work Stage 2: moderate but cannot work Stage 3: severe, cannot work, major intellectual disability Stage 4: vegetative (in AIDS dementia complex, a "vegetative" patient can be aroused to a level of alertness. This is an important distinction between AIDS dementia complex and many other potential etiologies.) [CSF abnormalities: pleocytosis, ↑ protein or ↑ immunoglobulin levels reported in 30% asymptomatic HIV+ individuals (<i>J Inf Dis</i> 158:193, 1988)]	Process is slowly progressive, weeks to months (usually occurs after AIDS defining diagnosis) and CD4 count usually < 200/mm ³ Neuro exam: non-focal <table border="1"> <tr> <td>Cognition</td><td>Early</td><td>Late</td></tr> <tr> <td></td><td>Inattention ↓ Concentration Forgetfulness, slowing of thought processing</td><td>Global dementia</td></tr> <tr> <td>Motor</td><td>Slowed movements Clumsiness Ataxia</td><td>Paraplegia</td></tr> <tr> <td>Behavior</td><td>Apathy Blunting of personality Agitation</td><td>Mutism</td></tr> </table> MRI scan: Early are typically normal. Cerebral atrophy, occasionally with diffuse fluid ("spilled milk"), edema of antral white matter and basal ganglia, best seen on T-2 weighted imaging. Normal gadolinium rules out most cases of primary brain lymphoma and toxo but does not rule out other infections (neurosyphilis, cryptococcal meningitis, MAI encephalitis) CSF: Relatively normal	Cognition	Early	Late		Inattention ↓ Concentration Forgetfulness, slowing of thought processing	Global dementia	Motor	Slowed movements Clumsiness Ataxia	Paraplegia	Behavior	Apathy Blunting of personality Agitation	Mutism
Cognition	Early	Late												
	Inattention ↓ Concentration Forgetfulness, slowing of thought processing	Global dementia												
Motor	Slowed movements Clumsiness Ataxia	Paraplegia												
Behavior	Apathy Blunting of personality Agitation	Mutism												
	Depression or anxiety	Sleep inversion, neuropsychiatric testing (Beck Depression Inventory)—most helpful in equivocal cases. See Table 7B, page 53												
	Neurosyphilis	CSF VDRL [sensitivity ranges from 10–89% (<i>Clin Inf Dis</i> 18:288, 1994)]												
	Adverse effects of sedative-hypnotic drugs	History												
	Alcohol/drug misuse	History												
	Non-HIV related causes: hypothyroidism, vitamin B12 deficiency, hypoxemia	Appropriate tests												

Abbreviations: MRI = magnetic resonance imaging, CT = computed tomographic scan, CSF = cerebrospinal fluid, CRAG = cryptococcal antigen, AFB = acid-fast bacilli, CD4 = T helper lymphocytes, VDRL = a reaginic antibody test (Venereal Disease Research Lab), > = greater than, < = less than

* These summaries have extensively utilized the 4th Edition of *The Medical Management of AIDS*, edited by Merle A. Sande and Paul A. Volberding, W.B. Saunders & Co., 1994. See Table 8 for details of treatment/disease entity.

** Adapted from R.W. Price and J.M. Worley, *ibid*.

TABLE 7A (2)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Central Nervous System (<i>continued</i>)	AIDS dementia complex (as above, Stage 3 or 4)	Course: ZDV can reduce prevalence of dementia in pts with HIV brain lesions but benefits disappear after about 12 months rx (<i>J AIDS</i> 6:42, 1993).
	Metabolic encephalopathies: Hypoxemic Sepsis Drugs	Exclude systemic factors
	Toxoplasmic encephalitis	Clinical: Usually subacute Serum antibody titer positive (> 85%) MRI: See below: focal brain disease
	Primary CNS lymphoma	Clinical: Rare without focal findings, which occur when deep structures in brain involved MRI: Single (most often) or multiple, hypodense, contrast-enhancing lesions. Both clinical presentation, CT, and MRI frequently indistinguishable from toxoplasmic encephalitis.
	Cytomegalovirus (CMV) encephalitis	Frequency and role still undefined MRI: Periventricular ependymitis
	Herpes simplex virus (HSV) encephalitis	Frequency and role still undefined CSF: Virus seldom cultured from CSF. Definitive dx requires brain biopsy (CSF PCR test in developmental stage)
	Arboviral encephalitis	Can occur in HIV+ individuals, may be independent. St. Louis encephalitis reported (<i>Clin Inf Dis</i> 17:140, 1993)
Focal brain disease: seizures and/or focal neurologic findings (hemiparesis, cerebrovascular abnormalities, blindness) Abrupt onset	Cerebrovascular event Transient ischemic attack (TIA) Cerebrovascular accident (stroke, CVA)	Clinical: Most TIAs are "benign", etiology is unknown. Exclude meningovascular syphilis. Inquire as to cocaine use with resulting risk of vasospasm ischemic events.
	Focal infection or neoplasm	See below
	Subacute course (days)	Toxoplasmosis [In U.S., occurs in 3-10% of patients with AIDS, in Europe and Africa occurs in 25-50% (<i>NEJM</i> 329:995, 1993). Frequency ↓ with use of TMP/SMX prophylaxis vs <i>P. carinii</i>] Clinical: Altered mental status (70%), hemiparesis and/or other focal signs (60%), headache (50%), seizures (30%). Fever, confusion, coma also seen. Toxoplasma serum IgG antibody titer negative in up to 16% (<i>NEJM</i> 327:643, 1992) Scan: MRI more sensitive than CT. MRI not always necessary if multiple lesions seen on CT. Multiple spherical ring enhancing lesions in basal ganglia and cortex, mass effect common. Lesions often identified without concomitant neurologic findings. Course: 70-85% will respond to specific anti-toxo treatment. In one series, 86% responded by day 7 (<i>NEJM</i> 329:95, 1993). If no improvement after 10-14 days of rx-biopsy. In 22 "non-responsive" cases, primary lymphoma in 10; treatable diagnosis in 16 (<i>West J Med</i> 158:249, 1993). Brain biopsy indicated earlier (in 7-14 days) in patients with early AIDS and/or good quality of life or if negative toxo antibody titer, single lesion and progression of symptoms on antitoxo rx. If improvement at 14 days, biopsy not required (<i>Lancet</i> 340:1135, 1992).

Abbreviations: CNS = central nervous system, PCR = polymerase chain reaction, dx = diagnosis, rx = treatment

TABLE 7A (3)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Central Nervous System (continued) Focal brain diseases: seizures and/or focal neurologic findings (continued) Subacute course (days) (continued)	Primary CNS lymphoma	Clinical: Usually afebrile. Often alert, but with mass effect may have more global mental dysfunction. Scan: White matter more often involved than gray matter. One or a few weakly enhancing irregular lesions, typically in periventricular region with mass effect. Thick-walled lesions are more common in lymphoma than in toxo (<i>Radiol</i> 179:823, 1991). Biopsy necessary for diagnosis.
	Tuberculous brain abscess (Meningitis, below)	Clinical: Evidence of extracranial infection may be absent.
	Cryptococcoma (Meningitis, below)	Clinical: Usually concomitant with cryptococcal meningitis. CRAG of CSF and serum often positive. But when an isolated occurrence, CRAG (serum and CSF) may be negative.
	Vaccinia zoster virus (VZV) encephalitis	Clinical: Often associated with dermatomal zoster. Scan: Multifocal infection of white matter similar to PML or vasculitis resulting in other findings. CSF: Virus may be isolated.
	Herpes simplex virus (HSV) encephalitis	See page 22
	Bacillary angiomatosis, intracerebral	Clinical: Very rare but treatable. Associated with other lesions (skin, liver). Scan: Contrast-enhancing mass lesion. Course: Responds to erythromycin (<i>Ann Int Med</i> 116:740, 1992)
	Chagas' Disease (<i>Trypanosoma cruzi</i>)	Clinical: One case report with hemiparesis. Born in El Salvador, in U.S. 6 years before onset of illness (<i>Am J Med</i> 92:429, 1992). Rare etiologies such as this emphasize the importance of brain biopsy.
Chronic course (weeks)	Progressive multifocal leukoencephalopathy (PML) (occurs in 4–7% of AIDS patients). Caused by JC virus (a papovavirus) (CD4 usually $\leq 200/\text{mm}^3$)	Clinical: Develops insidiously with a single focus (limb weakness, ataxia, visual disturbance). With progression, multiple foci occur. Preservation of alertness until late and without fever (<i>AIDS Clin Care</i> 5:17, 1998). MRI Scan: Multiple fluffy or diffuse hypodense non-contrast enhancing lesions in subcortical white matter, no mass effect. High signal intensity on T2 images in hemispheric white matter, ill-defined margins (CT/MRI—clinical dissociation). Lab: JC IgM antibody and PCR being investigated. Brain biopsy is definitive diagnostic procedure, sensitivity 40–96%, but not required if MRI is characteristic. CSF: Normal Course: Possible response to IV and intrathecal cytarabine but seen in only 1 of 8 patients (<i>Lancet</i> 342:622, 1993). Death usual within 6 months but spontaneous sustained remissions occur in 5–10% (<i>Neurol</i> 38:1060, 1988).
Seizures	Cerebral mass lesions (32%) Encephalopathy (24%) Meningitis (16%) Other or undetermined etiology (28%)	Cerebral mass lesions: majority are probable toxoplasma (<i>Am J Med</i> 87:173, 1989)

Abbreviations: PML = progressive multifocal leukoencephalopathy, $\leq$ = equal to or less than

TABLE 7A (4)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Central Nervous System (continued)		
Headaches	HIV-associated	May be a presenting symptom. Not AIDS dementia complex or HIV-associated aseptic meningitis. CSF: 0 pleocytosis (<i>Neural</i> 43:1098, 1993).
Meningitis (headache, fever, lethargy with or without nuchal rigidity)	Cryptococcal meningitis (CD4 usually $\leq 100/\text{mm}^3$)	Clinical: Stiff neck in only 1/4 of patients, focal findings in 1/5. 2/3 pts have extrameningeal cryptococcosis. LP opening pressure > 200 in 60% pts. Lab: CRAG (serum) $> 98\%$ positive. CSF: Often non-inflammatory. Median of 4 lymphs/ mm^3 , glucose normal to low, protein normal to $\uparrow$. India ink prep 75% sensitive. CSF CRAG $> 90\%$ sensitive. Increased intracranial pressure may be associated with blindness and $\uparrow$ mortality. If opening pressure $> 300 \text{ mmH}_2\text{O}$, urgently rx with CSF drainage. Dexamethasone or mannitol of questionable value.
	Bacterial meningitis (occurs at any CD4 level) Streptococcus pneumoniae Haemophilus influenzae Neisseria meningitidis	Clinical: Presentation similar to non-HIV+ population. Blood cultures usually positive.
	Listeria monocytogenes	Incidence of listeriosis (meningitis and bacteremia) 65–145X more common than in general population (<i>Clin Inf Dis</i> 17:224, 1993). Yield from blood cultures $\uparrow$ by "cold shock" of cultures, i.e., refrigerate overnight before incubation.
	Tuberculous (Mycobacterium tuberculosis)	Clinical: HIV+ at $\uparrow$ risk but clinical manifestations are similar to HIV- patients (<i>NEJM</i> 326:668, 1992) except intracerebral mass lesions more common (<i>Ann J Med</i> 93:520, 1992). CSF: Lymphocytic pleocytosis, glucose normal or $\downarrow$. May resemble cryptococcal meningitis but CRAG negative.
	Coccidioidal or histoplasma meningitis	Clinical: Uncommon but occur.
	HIV aseptic meningitis	Clinical: May occur early in HIV infection or relapsing throughout course. CSF: Mild lymphocytic pleocytosis, modest $\uparrow$ protein. These findings may be present in asymptomatic patient.
	Meningovascular syphilis	Clinical: May present with focal neurologic findings due to active endarteritis. Lab: CSF VDRL positive (serum VDRL may be negative). CSF glucose may be $\downarrow$.
Myelopathy		
Segmental, acute or subacute	Varicella-zoster virus (VZV)	Clinical: May be accompanied by dermatomal zoster
Transverse myelitis	Lymphoma, epidural or intradural	Scan: Shows mass
	Toxoplasmosis	See above, focal brain disease, subacute

Abbreviation: VZV = varicella-zoster virus

TABLE 7A (5)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Central Nervous System (continued) Myelopathy (continued) Segmental, acute or subacute (cont') With polyradiculopathy, includes cauda equina syndrome	Cytomegalovirus (CMV)	Clinical: Onset with paresthesias on soles of feet and perineum, and urinary retention. Bilateral leg pain, rapid flaccid paraparesis. Sensory findings less than motor. Reflexes ↓, no Babinski's. Arm weakness only late. CSF: Resembles bacterial meningitis, av. WBC 500/mm ³ with 71% PMNs, av. glucose 29 mg/dl, protein 270 mg/dl (<i>Neurol</i> 40:569, 1990). CMV culture + in 50–60%. Course: Response to ganciclovir equivocal, occasional patient responds, many do not.
	Herpes simplex virus II (HSV II)	Clinical: Transient sacral myeloradiculitis common. Also reported with progressive ascending myelitis. Combined HSV and CMV reported. CSF: Culture may be + for HSV.
Diffuse, subacute or chronic, progressive	Vacuolar myelopathy	Clinical: Usually associated with AIDS dementia. Stiffness, weakness, numbness in legs. Babinski's sign present. Progressive painless ataxia and spasticity. Bladder involvement late. Usually no distinct sensory or motor "level". CSF: Zero or 5–10 cells/mm ³ , ↑ protein Scan: MRI usually normal Course: No specific rx
	HTLV-I myelopathy	Clinical: "Tropical" spastic paraparesis CSF: Usually normal Lab: HTLV-I serology positive
Peripheral neuropathy [Useful diagnostic tests: EMG, nerve conduction studies, nerve biopsy] During acute HIV (seroconversion phase)	Mononeuritis—brachial plexopathy	Clinical: Acute onset, associated with "mononucleosis-like" syndrome. Recovery within several weeks. CSF: Minor lymphocytic pleocytosis Electrophysiologic studies: Helpful but not essential, both sensory and motor fibers affected (suggestive of a dying-back axonopathy). Biopsy: Axonal degeneration, sometimes with segmental demyelination.
CD4 > 500/mm ³	Acute demyelinating polyneuropathy (Guillain-Barre syndrome) Chronic inflammatory demyelinating polyneuropathy (CIDP) Multiple sclerosis-like illness	Clinical: Believed to have an autoimmune basis. May respond to plasmapheresis and/or corticosteroids. IVIG has been used, value unproven.
CD4 200–500/mm ³	Herpes zoster	Clinical: Recently reported with waxing and waning course. May respond to corticosteroids; if used, initial rx should be IV.
	Mononeuritis, multiplex	Clinical: 5–10% of patients develop VZV radiculitis.
CD4 < 200/mm ³	Mononeuritis, multiplex	Clinical: Occurs early and often benign. May relate to autoimmune vascular lesion.
	CMV ascending polyradiculopathy	See CMV myelopathy, above

Abbreviations: HTLV-1 = human lymphotropic virus type 1, PMN = polymorphonuclear leucocytes

TABLE 7A (6)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Central Nervous System (continued)		
Peripheral neuropathy (continued) Painful paresthesias	Predominantly sensory neuropathy or distal symmetric polyneuropathy	Clinical: Occurs in > 30% pts with AIDS. Early in course may be limited to soles of feet ("burning," "tingling"). May develop hyperalgesia. Symptoms rarely above knees. Muscle weakness, bladder and bowel dysfunction not a feature. Abnormal sensory exam on feet. Vibratory sense ↓, ↓ ankle jerks. Pathogenesis uncertain. May be due to direct HIV-1 infection. Does not respond to zidovudine. Rx with tricyclic antidepressants or analgesics (<i>AIDS Clin Care</i> 6:9, 1994).
	Tarsal tunnel syndrome	Sensory symptoms limited to anterior portion of the sole of the foot while the top of the foot is spared. Tinel's sign + (tap just below medial malleolus).
	Anti-retroviral drug-associated: zalcitabine (ddC), stavudine (d4T), didanosine (ddI), lamivudine (3TC), zidovudine (ZDV) (least common)	Clinical: Dose-related, may worsen for up to 4 weeks after discontinuation of rx.
	Other drug-associated	Neurotoxic drugs commonly used by HIV+ individuals: metronidazole, INH, dapsone, vincristine
	Metabolic neuropathies	Diabetes mellitus, alcohol, vitamin B ₁₂ deficiency, hypothyroidism
Autonomic Neuropathy [Cardiovascular autonomic tests: heart rate response to standing, heart rate variation during deep breathing, blood pressure response to sustained hand grip]		Clinical: Occurs in 30-60% with late disease. Abnormal sweating (↓ of feet, ↑ of upper body), postural hypotension, diarrhea or constipation, bladder dysfunction (<i>Arch Int Med</i> 151:2447, 1991).
Electrolyte and Metabolic Abnormalities		
Hyponatremia	Volume depletion 2° to diarrhea Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (2° to pulmonary or CNS infections) Adrenal insufficiency, primary Hyporeninemic hypoaldosteronism Nephrotoxic drugs: pentamidine, amphotericin B	Clinical: About 20% of ambulatory and 50% of hospitalized patients have serum Na of < 135 mmol/L. On admission ½ due to GI loss and hypovolemia. During hospitalization ½ due to SIADH (PCP, bacterial pneumonias, CNS infection). Patients are edema-free, with hypertonic urine with low serum osmolality and high urinary sodium (<i>Am J Med</i> 94:169, 1993).
Hyperkalemia	Trimethoprim Adrenal insufficiency Hypoaldosteronism Ketoconazole	Clinical: 20-53% pts on TMP/SMX or TMP + dapsone for treatment of PCP develop hyperkalemia. TMP is a sodium channel inhibitor and functions as a K-sparing diuretic agent (<i>NEJM</i> 328:703, 1993).
Hypercalcemia	Lymphoma	Lab: ↑ serum 1,25-dihydroxy vitamin D concentrations.
Hypocalcemia	Drug-related: Foscamet, ketoconazole, amphotericin B, aminoglycosides	Clinical: Neuromuscular irritability, carpal or pedal spasm. Foscamet forms complex with ionized calcium. Ketoconazole can block formation of 1,25-dihydroxy vitamin D (<i>NEJM</i> 327:1360, 1992). Ampho B and aminoglycosides may lead to Mg ⁺⁺ wasting with inhibition of parathyroid hormone release and action (<i>Arch Int Med</i> 151:1441, 1991).

Abbreviations: PCP = *Pneumocystis carinii* pneumonia; 2° = secondary; TMP/SMX = trimethoprim/sulfamethoxazole

TABLE 7A (7)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Electrolyte and Metabolic Abnormalities (continued)		
Lactic acidosis	Dideoxynucleoside (zidovudine, ddI, ddC) associated lactic acidosis (? idiopathic) Tissue hypoxia (Type A)	Clinical: Nausea, vomiting, fever, tachypnea with dyspnea. Arterial O ₂ saturation normal. Blood lactate > 5 mmol/L. Hepatomegaly with steatosis reported. Occurs disproportionately in obese women, see page 41. Resembles adult Reye syndrome. Mortality ~ 50% (<i>Ann Int Med</i> 118:37, 1993; <i>AIDS</i> 7:379, 1993).
Protein catabolism		Clinical: In patients with AIDS and secondary infections, caloric intake ↓ but there is no compensatory ↓ in energy expenditure (<i>NEJM</i> 327:329, 1992). See Systemic, wasting syndromes, page 52.
Endocrine System		
Pituitary gland [Useful diagnostic tests: Corticotropin releasing hormone (CRH) test; testing for several hormones simultaneously; insulin + thyrotropin releasing hormone (TRH) + gonadorelin (GnRH); measure glucose, cortisol, GH, TSH, prolactin, LH, FSH and ACTH]	Infectious involvement of anterior pituitary: CMV, P. carinii, Toxoplasma gondii	Clinical: 25% of advanced but non-AIDS HIV+ patients have ↓ pituitary reserve (<i>Am J Med Sci</i> 305:321, 1993). Functional pituitary insufficiency is very uncommon but reported (<i>Am J Med</i> 77:760, 1984).
Thyroid gland [Useful diagnostic tests: T ₃ , T ₄ , thyroid-binding globulin, rT ₃ (reverse T ₃)]	Chronic illness HIV infection	Lab: ↓ T ₃ with reciprocal ↑ rT ₃ , T ₄ usually normal Lab: Normal thyroid function reported. Serum T ₃ concentrations less low than seen in patients equally ill with other diseases. Thyroxine-binding globulin ↑ (<i>NEJM</i> 327:1360, 1992).
Adrenal gland [Useful diagnostic tests: AM, PM plasma cortisol levels; single dose cosyntropin stimulation test; plasma ACTH levels (if not available, metopirone test)]	Primary adrenal failure - CMV adenitis (found in 33–88% of AIDS pts at autopsy) - HIV infection of adrenal - Infiltration by Kaposi's sarcoma, lymphoma or infection (MAI, crypto, histo, pneumocystis) - Drug-induced: ketoconazole (impairs steroid synthesis), rifampin (induces hepatic enzymes which ↑ metabolism of steroids) Pituitary insufficiency	The adrenal gland is the most commonly affected endocrine gland in AIDS but frank Addison's disease is uncommon, although blunted responses to ACTH are common (<i>Am J Med Sci</i> 305:321, 1993). Clinical: Addison's disease: fever, hypotension, abdominal pain, hyponatremia, hyperkalemia. Addisonian crisis may be precipitated by excessive stress or ketoconazole. Patients with suboptimal response to ACTH stimulation should receive stress doses of corticosteroids in settings of infection, trauma, etc.
Pancreas [Useful diagnostic test: Serum glucose]	Drug-associated pancreatitis: pentamidine, didanosine (ddI), zalcitabine (ddC)	Clinical: Type I diabetes mellitus may develop.
Hyperglycemia	Drug-induced	Diabetogenic drugs frequently taken by HIV+ patients: dapsone, rifampin, sulfamethoxazole in patients with renal failure, octreotide, ganciclovir (<i>Ann Int Med</i> 118:529, 1993).

Abbreviations: MAI = Mycobacterium avium-intracellulare

TABLE 7A (8)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Endocrine System (<i>continued</i>)		
Gonads		
Testes		
[Useful diagnostic tests: Serum testosterone, LH, FSH, gonadorelin (GnRH) stimulation]	Primary testicular failure Drug-associated: ketoconazole	Clinical: ↓ libido and impotence common. Gynecomastia. Lab: ↓ testosterone levels, ↑ LH and FSH, normal GnRH response. Histology: Testicular abnormalities and ↓ spermatogenesis common.
Ovaries		Clinical: Information on gonadal function is available only for men.
Eye [Useful diagnostic tests: Ophthalmoscopic, slit lamp examinations, corneal scrapings, cultures, VDRL and FTA/ABS or MHA-TP]		
Anterior Segment Infections	Fungal keratitis, candida sp.	Clinical: Often no history of trauma, spontaneous and bilateral ulcers. Dx based on corneal scrapings and culture.
	Herpes simplex virus	Clinical: Predilection for peripheral rather than central involvement. Lesions take longer to heal and recurrences common. Dx: Fluorescein + epithelial "dendrites".
	Varicella zoster virus	Clinical: Most patients have H. zoster lesions in trigeminal nerve (1st division) distribution. 2/3 have keratitis, usually punctate.
	Corneal microsporidiosis (<i>Encephalitozoon hellem</i>) (<i>J Infect</i> 27:229, 1993)	Clinical: Photophobia, dry eyes, foreign body sensation, blurred vision. Punctate keratopathy. Pets, especially birds, suspected source. Nasal sinus epithelium occasionally involved. Dx: epithelial scrapings (<i>Am J Ophthalmol</i> 115:285, 1993).
	Chronic follicular conjunctivitis due to Molluscum contagiosum	Clinical: Lesions larger, more numerous, more rapid in onset than in immunocompetent individuals.
Posterior Segment Infections [At least 12 infectious agents identified as causes of retinal or choroidal disease in HIV+ patients (<i>ID Clin NA</i> 6:909, 1992). Considerations include more common or major entities]	HIV-associated "cotton wool" spots	Clinical: Usually asymptomatic. Ophthalm. exam: Small fluffy white lesions with indistinct margins without exudates or hemorrhages. Lesions do not progress and usually regress spontaneously.
	Cytomegalovirus (CMV) retinopathy Peripheral retinitis	Clinical: Occurs in 20–30% of AIDS patients. CD4 count is usually < 50/mm ³ . Course: Usually begins with unilateral "floaters" to ↓ visual acuity to blindness. Ophthalm. exam: Findings are usually initially in the periphery, moving centrally until macula and/or optic disc involved. Lesions are large creamy to white areas with granular borders and perivascular exudates and hemorrhages ("cottage cheese and ketchup" appearance) with little overlying vitreous reaction. If redness or pain of the eye, photophobia or irregular-shaped pupil develops, suspect infection other than CMV retinopathy. Dx: Based on clinical features, not on cultures or antibody test. Rx: See Table 8, page 71.
	Primary CMV papillitis	Clinical: Rapid ↓ in visual acuity. Optic atrophy within 4 weeks. Consider pulsed systemic steroids + ganciclovir or foscarnet (<i>Am J Ophthalmol</i> 108:691, 1989). Dx and rx: See CMV peripheral retinitis, above.

Abbreviations: FTA/ABS = fluorescent treponemal antibody-absorbed test, MHA-TP = microhemagglutination—Treponema pallidum

TABLE 7A (9)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Eye (continued) Posterior Segment Infections (continued)		
	Varicella-zoster virus (VZV) retinitis	Clinical: May not be associated with cutaneous zoster. (1) Acute retinal necrosis (ARN) syndrome: rapidly progressive necrosis of peripheral retina (often 360°) with occlusive vasculopathy, marked vitreous and anterior chamber inflammation, optic neuritis and scleritis. Complete visual loss in almost all patients. (2) Ill-defined areas of peripheral retinal whitening without granular borders, minimal vitreous reaction, no pain or foveal lesions (confused with CMV).
	Toxoplasmic chorioretinitis	Clinical: Ocular involvement uncommon in AIDS. Lesions may be single or multifocal, usually discrete, perivascular in location. Pre-existing chorioretinal scars usually absent. Hemorrhages are absent or minimal. Vitritis and iridocyclitis (red, painful eye) are common. May occur without intracranial lesions. Lab: Antibody titers unreliable. Course: Response to rx usually good, prolonged suppression required. Oral steroids not used.
	Syphilis: iridocyclitis, vitritis, optic neuritis, chorioretinitis, or combinations of these	Clinical: In HIV+, syphilitic ocular disease is more common, more severe and often bilateral. Necrotizing retinitis with hemorrhage may be confused with CMV. Cream-colored posterior plaques may be seen with mucocutaneous lesions in 2° syphilis. Lab: Positive VDRL and FTA/ABS or MHA/TP on serum. Course: Rx failures reported.
	Choroidal pneumocystosis	Clinical: Almost all patients have had <i>P. carinii</i> pneumonia and prophylaxis with aerosolized pentamidine. Creamy to orange choroidal lesions, usually bilateral without vitreous inflammation. Visual acuity usually not affected. Course: Response to systemic rx usually good.
	Cryptococcosis: choroiditis, endophthalmitis	Clinical: In one series 9/27 (33%) pts with crypto meningitis had neuro-ophthal. signs (<i>Ophthalmology</i> 96:1092, 1989). Rapid visual loss with optic nerve involvement. May be due to ↑ intracranial pressure, a medical emergency—rx with CSF drainage. Multifocal white lesions with optic nerve edema usually without vitreous inflammation seen. Dx usually based on systemic and/or meningeal crypto. With rx, progressive optic atrophy may occur.
	Candidal endophthalmitis	Clinical: Prevalence in HIV+ pts unclear. It is rare with only mucocutaneous candidiasis, but may be associated with candidemia with IV lines and neutropenia. Well-demarcated yellow to white lesions which protrude into vitreous, not associated with hemorrhage and usually unilateral.
	Bacterial retinitis: <i>Mycobacterium avium-intracellulare</i> , <i>Rhodococcus equi</i> reported	
	Retinal depigmentation	Clinical: 5% of children on didanosine (ddi) at > 300 mg/M ² /day developed retinal depigmentation. Asymptomatic.
	Retinal deposits of clofazimine	Clinical: Clofazimine deposits in pigmented tissues. May result in brownish refractile crystals in retina.

TABLE 7A (10)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Fever, night sweats, weight loss, with or without diarrhea [Useful diagnostic test: blood cultures]	Viral: Cytomegalovirus Bacterial: MAI, tuberculosis, bacillary angiomatosis, salmonella, infective endocarditis in drug users. Fungal: Histoplasmosis, coccidioidomycosis, cryptococcosis Parasitic: Pneumocystis carinii, toxoplasmosis Neoplasms: Lymphoma, Kaposi's sarcoma	In pts with CD4 < 200, fever is common (46% of patients over 9 months). HIV virus as sole etiology unusual. If > 2 weeks required to make diagnosis (22% of febrile pts): MAI, P. carinii pneumonia (on aerosol pentamidine), non-Hodgkin's lymphoma most common. If < 2 weeks required to make dx: 29% PCP, MAI, toxo, non-Hodgkin's lymphoma; 34% associated with HIV or rx—catheter-related bacteremia, bacterial pneumonia, drug allergy, sinusitis; 15% non-related diagnosis, e.g., bronchitis (<i>Arch Int Med</i> 153:1909, 1993).
Gastrointestinal Tract		
Mouth* [Useful diagnostic tests: Physical examination; exudate/membrane—KOH preparation for yeast, culture for virus, fungi; biopsy—stain: H&E, PAS, GMS] Oral lesions with or without soreness	Primary (seroconversion) HIV disease	Clinical: Oral ulcerations in 12/30 pts (40%), enanthemas (40%), 5 pts had both (<i>Clin Inf Dis</i> 17:59, 1993). Lab: Thrombocytopenia 74%. HIV antibody test initially + in 7/30 (23%).
	Candidiasis Pseudomembranous form (thrush)	Clinical: Small 1–2 mm to large white plaques on any mucosal surface. Can be wiped off, leaving erythematous to bleeding base. Lab: Dx established by KOH prep of scraping and culture.
	Erythematous form	Clinical: Smooth red patches on soft or hard palate, dorsal tongue and/or buccal mucosa. Lab: Dx established as above.
	Angular cheilitis	Clinical: Erythematous cracks and fissures at corner of mouth. Lab: Dx established as above.
	Hyperkeratotic form (candidal leukoplakia)	Clinical: White lesions on tongue, palate and/or buccal mucosa that cannot be wiped off. Clinically resembles hairy leukoplakia (see below). Lab: Biopsy of lesion will show fungi.
	Kaposi's sarcoma	Clinical: Red to purple macules, papules or nodules, occasionally the same color as adjoining tissue, on tongue, palate or buccal mucosa. Usually asymptomatic but may become painful with ulceration and inflammation. Lab: Biopsy
	Hairy leukoplakia	Clinical: A sign of advancing HIV infection. Lesions usually asymptomatic. White thickening of oral mucosa and/or lateral tongue margins with vertical folds or corrugations. Lesions range from few mm to covering entire dorsal surface of the tongue. Has been associated with Epstein-Barr virus (EBV) and human papillomavirus (HPV) occasionally mixed with candida. Lab: Biopsy: epithelial hyperplasia with thickened parakeratin layer with hair-like projections and vacuolated prickly cells. Cannot be cultured on routine viral cultures. Rx: Usually not treated, but can be rx with high-dose acyclovir (see page 73). Lesions respond but recur. 10/10 pts responded to one application of topical podophyllin resin within 4–5 days, remissions of 2–28 weeks (<i>J AIDS</i> 4:543, 1991).

* Adapted from J.S. Greenspan, D. Greenspan, *Medical Management of AIDS*, 4th Ed. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994

Abbreviations: KOH = potassium hydroxide, H&E = hematoxylin and eosin, PAS = periodic acid Schiff stain, GMS = Gomori methenamine silver stain

TABLE 7A (11)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Gastrointestinal Tract (continued) Mouth (continued) Oral lesions with or without soreness (con't)	Warts [human papillomavirus (HPV)]	Clinical: Usually asymptomatic. Present as single or multiple papilliform warts with multiple white spike-like projections or as pink cauliflower masses or as flat lesions resembling focal epithelial hyperplasia. Lab: Biopsy
	Lymphoma	Clinical: Poorly demarcated swelling on alveolar ridges and/or discrete oral masses. Lab: Biopsy
	Carcinoma, squamous cell	Clinical: Squamous cell carcinoma of tongue reported in HIV disease. Lab: Biopsy
	Cytomegalovirus (CMV) oral ulcers	Clinical: A rare manifestation of CMV (<i>Ann Int Med</i> 119:924, 1993) Lab: Biopsy
	Histoplasmosis, Geotrichosis, Cryptococcosis	Clinical: Rare in occurrence. Lesions are not clinically typical. Lab: Biopsy; organism identified on culture and stains.
Sore mouth without discrete lesions	HIV-associated gingivitis and periodontitis	Clinical: Common with advanced HIV. Marked halitosis, spontaneous bleeding and deep-seated gingival pain are usual. Gingiva show fiery red margins with necrosis and ulceration of interdental papillae. May rapidly progress to loss of gingival soft tissue and destruction of supporting bone leading to loss of teeth and necrotizing stomatitis. Is similar to noma (gangrenous stomatitis). Dx: Based on clinical features. Cultures not helpful. Rx: Start with curettage/debridement, followed by topical povidone-iodine (Betadine) irrigation, then chlorhexidine gluconate (Peridex) mouthwash + oral antibiotics effective against anaerobes (metronidazole, clindamycin, AM/CL).
Oral lesions, painful	Recurrent aphthous ulcers (RAU)	Clinical: RAU may be more common in HIV disease. Recurrent crops of superficial painful ulcers (1 mm to 1 cm) on non-keratinized oral or oropharyngeal mucosa. Lab: Biopsy; shows only non-specific inflammation. Rx: Topical steroids may ↓ pain and swelling.
	Herpes simplex virus (HSV)	Clinical: Recurrent crops of small painful vesicles that ulcerate, usually on palate or gingiva. Usually heal but tend to recur. Herpetic geometric glossitis [extremely tender longitudinal fissures occur, heal with acyclovir IV (<i>NEJM</i> 329:1859, 1993)]. Lab: Smears from lesions reveal multinucleate giant cells, + for HSV on immunofluorescent staining.
	Drug-associated lesions	Clinical: Painful mouth lesions occur in 10–15% of patients on zalcitabine (ddC), dapsone.
Xerostomia (dry mouth)	Sjogren's-like syndrome Drug-associated	Clinical: Dry mouth occurs in 2% of patients on didanosine (ddI). See <i>Salivary gland enlargement</i> , Table 7A, page 32
Osteomyelitis of the mandible		Described in 3 HIV+ pts. Presented as pain, swelling. X-ray findings in only 1 pt. Cultures done late. (<i>S Med J</i> 86:1215, 1993).

Abbreviations: AM/CL = amoxicillin clavulanate

TABLE 7A (12)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Gastrointestinal Tract (continued) Salivary gland enlargement	Benign parotid lymphoepithelial lesions (diffuse infiltrative CD8 lymphocytosis syndrome)	Clinical: Presents as painless (80%) bilateral parotid swelling due to infiltration with CD8 + T lymphocytes. Submandibular glands not involved. CD4 counts 200–500/mm ³ . 80% have generalized lymphadenopathy, bilateral cervical. Resembles Sjogren's syndrome with sicca symptoms (dry mouth and eyes). Associated findings may include lymphocytic interstitial pneumonia (60%), aseptic meningitis. Most black pts were HLA-DR5. In contrast to Sjogren's, none had anti Ro/SS-A or anti La/SS-B antibodies, rheumatoid factor usually negative. Dx based on fine needle aspiration. Rx with zidovudine (<i>Ann Int Med</i> 112:3, 1990; <i>Am J Surg</i> 162:324, 1991).
Esophagus* [Useful diagnostic tests: X-ray—barium swallow; endoscopy—direct brushing, biopsy (histology, culture—viral, fungal)]		
Dysphagia (difficulty swallowing with a sensation of food sticking)	Candidiasis	Clinical: The most common cause of dysphagia in HIV+ patients (42–79% of pts). X-ray: Barium swallow; typically evidence of plaques and ulceration ("moth-eaten" appearance). Findings supportive but not diagnostic. Endoscopy: In HIV+ pt with new onset dysphagia/odynophagia, especially if oral thrush present, some authorities recommend 1–2 weeks of fluconazole or ketoconazole as initial management. If no response, then endoscope (<i>Am J Med</i> 92:412, 1992). Endo will typically show large yellow-white plaques usually throughout the esophagus. Biopsy/brushing: Will show tissue-invasive pseudomycelia. Secondary prophylaxis: Recurrence rates (20–80%) in 45–90 days. Fluconazole: dosage not defined; 100 mg po biweekly, 10% recurrence over median of 9 months (32nd ICAAC Abst 1116:297, 1992). 150 mg po weekly, 42% recurrence over 6 months (<i>Med J Aust</i> 158:312, 1993).
	Drug-associated	Clinical: Dysphagia occurs in 2–3% of patients on zalcitabine (ddC).
Odynophagia (pain on swallowing) or esophagospasm (retrosteral episodic pain without swallowing)	Esophageal ulcers associated with HIV seroconversion	Clinical: Seroconversion symptoms (fever, myalgia, maculopapular rash) + odynophagia or dysphagia (<i>JAMA</i> 263:2318, 1990). Lesions heal spontaneously. These pts are not predisposed to recurrent esophageal ulceration. Endoscopy: One or more discrete ulcers. On biopsy: retroviral virions. Rx: Viscous lidocaine may ↓ symptoms.
	Cytomegalovirus (CMV) esophagitis	Clinical: Common 8–13% HIV+ pts. Symptoms are odynophagia, usually without dysphagia, weight loss. Endoscopy: Large solitary (> 10 cm ² in surface area), shallow, superficial ulcers especially in the distal esophagus (<i>Ann Int Med</i> 113:589, 1990). Histology necessary to establish diagnosis. Rx: Therapeutic trial with ganciclovir in symptomatic patient may be warranted but toxicity may outweigh benefit. Stricture may occur after healing.
	Idiopathic (aphthous) esophageal ulceration (IEU)	Clinical: In one series, 1/3 pts with esophageal ulcers due to IEU. Pts present with odynophagia. CMV, HSV, drug-induced ulcers. Endoscopy: Large discrete ulcers. Rx: Prednisone 40 mg po qd, taper by 10 mg/week, total course 4 weeks. 11/12 pts responded clinically (<i>Am J Med</i> 93:131, 1992).

* Adapted from J.P. Cello, *Medical Management of AIDS*, 4th Ed. Eds.: M.A. Sande, P.A. Volberding. W.B. Saunders & Co., 1994.

TABLE 7A (13)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Gastrointestinal Tract (<i>continued</i>)		
Esophagus (<i>continued</i>)	Herpes simplex virus (HSV) esophagitis	Endoscopy: Fewer, smaller (1–2 cm), deeper ulcers than with CMV. Rx: Acyclovir
Odynophagia (<i>continued</i>)	Lymphoma, Kaposi's sarcoma, squamous cell carcinoma, histoplasmosis	Clinical: Occur occasionally in esophagus in HIV.
Stomach (nausea, vomiting, early satiety, hematemesis, melena) [Useful diagnostic tests: Physical exam—stool guaiac; x-ray—upper GI series; endoscopy—biopsy (histology; immunohistologic studies; culture, viral)]	Kaposi's sarcoma (KS)	Clinical: Occurs in 40% of patients with cutaneous or nodal KS. Usually asymptomatic, occasional hematemesis. Endoscopy: Submucosal reddish nodules with intact overlying mucosa. Biopsy necessary to confirm dx but many lesions (3/4) cannot be biopsied because of submucosal location and limited depth of endoscopic biopsies.
	Lymphoma	Clinical: May produce obstructed gastric outlet syndrome or hemorrhage (hematemesis, melena). In HIV lymphomas often multifocal with disease throughout abdomen. X-ray: Larger masses often show "target lesions" with central umbilicated ulcerations. Endoscopy: Mass lesions, biopsy
	Cytomegalovirus (CMV) gastritis	Endoscopy: See CMV esophagitis above, lesions are similar
	Gastric ulcer, duodenal ulcer, duodenitis	Clinical: Consider antiretroviral drugs as the cause: zidovudine (500 mg/d, dyspepsia 6%), didanosine (250 mg bid, abdominal pain 7%), zalcitabine (0.75 mg q8h, abdominal pain 3%), foscarnet (60 mg/kg IV q8h, abdominal pain ~5%); drugs for opportunistic infection: TMP/SMX, ketoconazole, fluconazole, neomacrolides (abdominal pain 2–3%); other drugs, especially NSAIDs.
Abdominal pain, acute onset	Pancreatitis	Drug-associated
	Bowel perforation	AIDS pts with perforation are usually febrile, with rigid abdomen and rebound tenderness. Perforations most common in large bowel. Most common etiology is CMV. Also lymphoma, typhilitis, KS, tuberculosis, salmonellosis (<i>Emerg Med Clin NA</i> 7:575, 1989).

TABLE 7A (14)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Gastrointestinal Tract (continued) Small bowel disease* (cramping paraumbilical abdominal pain, weight loss, large volume diarrhea. Diarrhea occurs in 30–60% of U.S. and European HIV+ patients and ~90% in developing countries.) [Useful diagnostic tests: Stool examination: Microscopic—methylene blue stain for fecal leukocytes, fresh mount and stain for parasites, modified AFB or immunofluorescent stain Culture—bacterial, <i>M. tuberculosis</i> and fungal <i>C. difficile</i> toxin assay Fecal fat determination Chromotrope stains for microsporidia (NEJM 326:161, 1992) Endoscopy—via colon or small bowel, biopsy]	Infectious agents associated with diarrhea in HIV+ patients in U.S. (AIDS enteropathy): Cytomegalovirus 5–45% Mycobacterium avium-intracellulare (MAI) 5–23% Salmonella (non-typhoid) 0–25% Cryptosporidia 5–15% Entamoeba histolytica 0–25% Giardia lamblia 2–15% Microsporidia (Enterocytozoon bienersi) 23–33% Campylobacter jejuni 4% Adenovirus 4% Isospora belli < 2% Clostridium difficile toxin 3% Candida sp. ? 3% Strongyloides stercoralis ? 3% Rotavirus < 1% Cyanobacterium incidence not defined (Cyclospora cayentensis) Novel enteric viruses (see Comments) No pathogen identified ~15%	Most patients with AIDS and chronic diarrhea have an opportunistic infection of the small bowel or colon. Studies of small bowel usually reveal villous atrophy and crypt hyperplasia, but found in AIDS pts without diarrhea and in other diseases, e.g., coeliac disease, malnutrition, chemotherapy, etc. Specific identification and treatment depends upon laboratory identification. Specific treatment, see Table 8. In patients with CD4 > 180/mm ³ , cryptosporidium cleared spontaneously in 7–28 days, with CD4 < 180, 87% persisted (Ann Int Med 116:840, 1992). Cyclospora cayentensis is the proposed name for cyanobacterium-like bodies (Lancet 341:1034, 1993). Cyclospora species more recently reported as a cause of diarrhea in immunocompetent individuals (in Peru, Nepal) and in U.S. as well as in AIDS (NEJM 328:1308, 1993). Novel enteric viruses found more commonly in HIV+ pts with diarrhea include astrovirus, picobornavirus, caliciviruses (NEJM 329:14, 1993).
Typhilitis	Diarrhea due to alternative mechanisms	Considerations: HIV disease per se, autonomic denervation (see CNS, page 26), Crohn's disease, lymphokines, overgrowth of normal microbial bowel flora. Clinical: Clinically resembles acute appendicitis, but involves the cecum, which is ulcerated, edematous, necrotic. Associated with Clostridium septicum and Pseudomonas aeruginosa (Ann Int Med 116:996, 1992). Can be a manifestation of <i>C. difficile</i> .
Colorectal disease (left lower quadrant and/or suprapubic cramping, rectal urgency (tenesmus), frequent small volume stools, occasional proctalgia and dyschezia (painful defecation)) [Useful diagnostic tests: Stool exam as above—herpes virus culture of perianal ulcer; endoscopy—flexible sigmoidoscopy, colonoscopy]	Drug-associated diarrhea Infectious agents (as above)	25 of 200 (12.5%) patients with diarrhea + for Clostridium difficile toxin, 18 of 25 had received antibiotics. Response to vancomycin or metronidazole less prompt (Clin Inf Dis 15:726, 1992).

* Adapted from J.G. Bartlett, et al., Clin Inf Dis 15:726, 1992, J.P. Cello, Medical Management of AIDS, 4th Ed., Edit. M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994, and P.D. Smith et al., Ann Int Med 116:63, 1992.

Abbreviations: AFB = acid-fast bacilli, mg/d = milligrams per day; TMP/SMX = trimethoprim/sulfamethoxazole; neomacrolides = azithromycin, clarithromycin; NSAIDs = non-steroidal anti-inflammatory drugs and salicylates

TABLE 7A (15)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Gastrointestinal Tract (continued)		
Colorectal disease (continued)	Cytomegalovirus (CMV)	Endoscopy: Focal ischemic colitis with submucosal hemorrhages and discrete shallow ulcers in distal colonic mucosa. Ganciclovir is effective in most patients (<i>J Inf Dis</i> 167:278, 1993).
	Herpes simplex virus (HSV) Types 1 & 2	Clinical: Painful recurrent small to persistent progressive large necrotizing ulcers in perirectal area. Lab: Smears from lesions reveal multinucleate giant cells, + for HSV on immunofluorescent staining.
	Mycobacterium tuberculosis	Clinical: Tuberculosis in ileocecal area and colon may be seen in HIV patients without evidence of pulmonary TB on chest x-ray.
	Other considerations: Idiopathic inflammatory bowel disease (ulcerative colitis), Kaposi's sarcoma, lymphoma, epidermoid carcinoma and other neoplasms	
Proctitis [Useful diagnostic tests: Proctoscopy with specimen for smear, culture, biopsy]	Neisseria gonorrhoeae Herpes simplex virus Syphilis, primary or secondary Lymphogranuloma venereum (LGV) Chlamydia trachomatis (non-LGV immunotypes) Human papillomaviruses Cytomegalovirus Enteric pathogens, e.g., Shigella, Entamoeba histolytica, Giardia lamblia, Campylobacter	Lab: Numerous PMNs on smear of exudate. Specific diagnosis depends on laboratory studies.
Genital Tract		
Anogenital warts (Condylomata acuminata) [Useful diagnostic tests: • RPR • Cervical warts: Pap smear • Atypical or persistent: biopsy]	Genital warts (human papillomavirus (HPV) types 6, 11, 16 and 18) Secondary syphilis, condyloma lata Carcinoma	Clinical: Soft, moist, pink or red swellings that grow rapidly. Usually several in same area and look like cauliflower. Identified clinically. Exclude condyloma lata of secondary syphilis. If atypical or persistent, biopsy to exclude carcinoma. Women with cervical warts should not be treated until result of Pap smear available. Rx: See Table 8, page 72
Gonorrhea [Useful diagnostic tests: • Gram stain of discharge • Culture of discharge and/or area on selective (e.g., Thayer Martin) medium • Fluorescent antibody stain for Chlamydia trachomatis • RPR]	Gonorrhea Non-gonococcal urethritis: Chlamydia trachomatis, Ureaplasma urealyticum	Clinical: Spontaneous purulent discharge Lab: Urethral smear usually shows > 95% PMNs. Gram stain: Gram-negative intracellular diplococci. 50% of patients with gonorrhea have concomitant C. trachomatis. Rx: See Table 8, page 61

Abbreviation: RPR = rapid plasma reagin test

TABLE 7A (16)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Genital Tract (continued) Non-gonococcal urethritis, cervicitis	Non-gonococcal urethritis: <i>C. trachomatis</i> (50%), other known etiologies (10–15%); <i>Ureaplasma urealyticum</i> . In women: Herpes simplex virus, trichomoniasis, candidiasis Gonorrhea	Clinical: Urethral discharge usually not spontaneous (no "drip"), thin, watery in character. Lab: Urethral smear usually shows < 80% PMNs + epithelial cells. Positive fluorescent antibody (FA) test vs. <i>C. trachomatis</i> . By EIA or PCR, <i>C. trachomatis</i> can be diagnosed in males with voided urine. 6–10% of ureaplasma are resistant to tetracycline (doxycycline). Rx: See Table 8, page 57
Syphilis [Useful diagnostic tests: • RPR, FTA/ABS, or MHA/TP • Darkfield exam of lesion (except intra-oral lesions)]	Syphilis in the HIV+ pt has been described with fulminant presentations, rapid progression, irregular serologic findings and failure of standard penicillin therapy. Yet others have reported that HIV has not altered clinical syphilis (<i>Ann Int Med</i> 118:350, 1993). Primary syphilis (chancre): other etiologies that cause ulcerative lesions—herpes, chancroid, scabies, granuloma inguinale, trauma. Uncommon; tuberculous ulceration, Behçet's, CMV. Drug reaction: foscarnet. Secondary syphilis: Can mimic most skin diseases. Common misdiagnoses include: drug eruption, rubella, infectious mononucleosis, fungal infection, primary (seroconversion) HIV. Condyloma lata confused with warts, hemorrhoids. Scalp lesions with ringworm, alopecia areata Latent [early, < 1 year's duration; late, > 1 year's duration, indeterminate, neurosyphilis]	Clinical: Syphilitic chancre not exquisitely tender. Dual infections, syphilis and herpes, not uncommon. All genital ulcers should be considered syphilitic until proven otherwise. Lab: RPR does not become + until 3–6 weeks after initial infection. An early negative test does not exclude syphilis. If negative, repeat at 6 weeks. The FTA/ABS becomes + at 3–4 weeks. Clinical: Usually associated with generalized lymphadenopathy. Patient often febrile. May show findings of hepatitis and/or nephritis. Lab: Positive darkfield. The RPR and FTA/ABS are virtually always positive. In pts with suggestive clinical findings and non-reactive RPR or VDRL dilute serum to exclude possible prozone phenomenon (<i>Arch Int Med</i> 153:2496, 1993). CDC recommends an LP (with CSF RPR) on all HIV+ patients with or without neurologic symptoms, or individuals with serum FTA/ABS antibody titer $\geq 1:32$, or individuals who will not be rx with penicillin. See Table 8. (<i>MMWR</i> 42:(RR-14) 39, 1993). Pts with reactive CSF VDRL tests are considered to have proven neurosyphilis (but sensitivity is 9–89%). Pts with reactive serum RPR and FTA/ABS (or VDRL and MHA-TP) and CSF pleocytosis or $\uparrow$ levels of protein are considered to have presumptive neurosyphilis. But in HIV+ individuals with no evidence of syphilis, 30% have CSF pleocytosis or $\uparrow$ protein (<i>Clin Inf Dis</i> 18:288, 1994). The diagnosis of neurosyphilis in HIV+ individuals is problematic.
Chancroid (<i>Haemophilus ducreyi</i>) [Useful diagnostic tests: • RPR, FTA/ABS, or MHA/TP • Culture from edge of lesion or bubo on medium supplemented with patient's own serum]	See primary syphilis	Clinical: Genital ulcers are exquisitely tender. Usually associated with suppurative of inguinal nodes. Upon exposure to HIV+ contact, HIV seroconversion occurred in 2.9% of men with genital ulcers vs 1.0% in those without ulcers (<i>Ann Int Med</i> 119:1181, 1993). Rx: See Table 8, page 57

Abbreviations: RPR = rapid plasma reagin test, FTA/ABS = fluorescent treponemal antibody-absorbed test, MHA/TP = microhemagglutination—*Treponema pallidum*, VDRL = Venereal Disease Research Lab (test), EIA = enzyme immunoassay, LP = lumbar puncture

TABLE 7A (17)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Genital Tract (<i>continued</i>)		
Lymphogranuloma venereum (LGV) - RPR, FTA/ABS - Complement fixation tests on serum, rising antibody titer vs Chlamydia trachomatis	"Viral syndromes" Ulcerative proctitis	Clinical: Small, transient non-indurated vesicular lesion which heals quickly and may be unrecognized. 1st symptom usually unilateral tender enlargement of inguinal nodes (avoid biopsy—may fistulate) which progresses to inflammation of overlying skin, multiple sinuses. Constitutional symptoms: fever, malaise, headache, joint pains are common. If rectum involved, bloody purulent rectal discharge.
Granuloma inguinale (Calymmatobacterium granulomatis) - RPR, FTA/ABS - Microscopic exam of scrapings from edge of lesion (Giemsa stain)	See <i>primary syphilis</i>	Clinical: Rare in the U.S. Initially a painless red nodule which slowly increases in size and ulcerates. No associated lymphadenopathy. Lab: Giemsa stain of scrapings: Donovan bodies, intracytoplasmic bacilli in macrophages. Rx: See Table 8, page 57
Genital herpes simplex (HSV) [usually type 2, but may be type 1 (~5%)] - RPR, FTA/ABS - Tzanck prep from lesion (multinucleate giant cells on Giemsa stain) - Viral culture	See <i>primary syphilis</i>	Clinical: Small painful vesicles, usually in clusters. Ulcerate and may coalesce into large lesions. Inguinal nodes usually slightly enlarged and tender. Usually heal in 10–20 days without scarring. In AIDS pt, recurrent genital herpes may be of ↑ severity with severe local pain, prolonged viral shedding and symptoms lasting weeks. Frequently result in large chronic ulcers in advanced HIV infection. Acyclovir resistance is common. Rx: See Table 8, page 72
Reiter's syndrome	See <i>Musculoskeletal System</i> , page 48	
Cervical dysplasia [Useful diagnostic tests: - Pap smear - Colposcopy with biopsy]	Cervical intraepithelial neoplasia (CIN)	Clinical: In one study 14/35 HIV+ had intraepithelial lesions vs 3/32 HIV- women (<i>J AIDS</i> 3:696, 1990). May be missed on Pap smear, colposcopy better (<i>Ob Gyn</i> 76:84, 1991).
Salpingitis-pelvic inflammatory disease (PID), salpingitis, tuboovarian abscess [Useful diagnostic test: Laparoscopy]	- Pelvic inflammatory disease: gonococcus, chlamydia, anaerobes (Bacteroides fragilis and other species), enterobacteriaceae, streptococci (especially Group B), mycoplasma - Appendicitis - Ectopic pregnancy	Clinical: PID is more serious in the HIV+ woman (7–17% require hospitalization). Indications to hospitalize: compliance as an outpatient unlikely, pregnant, peritonitis, suspected pelvic (tuboovarian) abscess, diagnosis uncertain, need for laparoscopy to clarify diagnosis, failure to respond on outpatient rx in 72 hours.
Vaginitis	Candidiasis	Candida vaginitis, recurrent and/or refractory, initial symptom of HIV infection in about 1/4 of women (<i>Am J Med</i> 89:142, 1990). Pruritus; thick cheesy discharge; pH 4.5; hyphae on KOH prep
	Trichomoniasis	Copious foamy discharge, pH 5–7, T. vaginalis on isotonic saline prep
	Bacterial vaginosis	Malodorous discharge; pH 5–6; wet prep shows cells covered with organisms "clue" cells. Fishy odor when secretions rx with KOH

Abbreviations: RPR and FTA/ABS, see page 36

TABLE 7A (18)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Genital Tract (continued) Scabies (Sarcoptes scabiei) (Norwegian scabies)	See Skin, page 51	
Pediculosis pubis (Phthirus pubis) (crabs)		Clinical: Itching in anogenital region. Scrotal dermatitis (excoriation) usually present. Ova (nits) attach to the skin at the base of the hairs. Minute brown spots on undergarments (louse excreta) may be seen.
Heart	Myocarditis [Useful diagnostic tests: ECG, MUGA scan]	At necropsy, 52% of 71 consecutive cases had evidence of minimal cardiac disease (<i>J Am Coll Cardiol</i> 11:792, 1988). Etiology remains undefined and is rarely clinically significant.
	Cardiomyopathy Idiopathic	Biventricular dilatation with pathologic features of myocarditis. Average ejection fraction 33% (<i>J Am Coll Cardiol</i> 13:1030, 1989). Etiology is unknown. Causal relationship to Coxsackie B, CMV and HIV not proven. No causal relationship to malnutrition, immunologic mechanisms. Rx is after load reduction and diuretics.
	Drug-associated	Clinical: ZDV and ddI—6 cases reported. CHF after 16 mos. rx, 2 associated with skeletal myositis (<i>Ann Int Med</i> 116:311, 1992). Patients improved after antiretroviral drugs discontinued. Recommend: Pts developing CHF, withdraw dideoxynucleoside rx for 1 month, then perform invasive cardiac function evaluation. Alfa interferon—Reversible cardiac dysfunction reported (<i>NEJM</i> 321:1246, 1989).
	Endocarditis; non-bacterial, thrombotic (marantic) [Useful diagnostic test: echocardiogram (transesophageal most sensitive)]	Sterile thrombi common, may be on any valve and embolize systemically. Opportunistic pathogens not a common cause of endocarditis in HIV+ patients (although there are case reports). Response of HIV+ patient to rx is similar to non-HIV+ patient.
	Infective	Consider in injection drug users, reported in 4–10%.
	Pericardial disease [Useful diagnostic tests: pericardiocentesis; culture, cytology]	Pericardial effusions are common. Tamponade is rare. Specific organisms include <i>M. tuberculosis</i> , <i>MAI</i> , <i>Cryptococcus</i> . Kaposi's sarcoma may involve the pericardium.
	Malignancy Kaposi's sarcoma Lymphoma	Lesions are clinically silent but may produce irritability with arrhythmias. Cardiac involvement with Kaposi's sarcoma or lymphoma usually occurs only with widespread disease.
Hematologic Abnormalities* Anemia (occurs in up to 85% of AIDS patients) [Useful diagnostic tests: • Hemolysis screen • Smear for RBC morphology • Reticulocyte count • Iron studies • Bone marrow]	Anemia of chronic disease (impaired erythropoiesis)	• Normochromic, normocytic • ↓ reticulocyte counts • ↓ erythropoietin levels (inappropriately low for degree of anemia) • ↓ serum iron, ↓ total iron-binding capacity (TIBC) • ↑ bone marrow iron stores
	Iron deficiency anemia secondary to GI bleeding (Kaposi's sarcoma, lymphoma, carcinoma)	• Microcytic, hypochromic • ↓ serum iron, ↑ TIBC • ↓ bone marrow iron stores

Abbreviations: MUGA = multiple gated acquisition scan, ECG = electrocardiogram.

* Adapted from J. Hambleton, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994; J.P. Doweiko, *Blood Rev* 7:121, 1993

TABLE 7A (19)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Hematologic Abnormalities (continued) Anemia (continued)	Infiltration of the bone marrow (especially <i>Mycobacterium avium</i>-intracellular) Decreased B₁₂ levels Antibody-mediated hemolysis Pure red cell aplasia due to parvovirus B-19 Drug-induced anemia • G6PD deficient hemolysis; common: dapsone, primaquine; uncommon: INH, sulfonamides, TMP/SMX • Zidovudine produces megaloblastic anemia	Anemia often profound (hematocrit 15–20%) Occur in 20%. Most likely due to altered serum transport. Anemia usually not due to or compounded by B₁₂ deficiency. Direct Coombs test commonly positive. Hemolysis is rare. Bone marrow shows maturation arrest at pronormoblast stage. Rx with IV immune globulin has resulted in cure or remission in most patients, enabling administration of full ZDV dosage. Zidovudine: May respond to epoetin alfa if endogenous serum erythropoietin levels $\leq$ 500 mU/ml and ZDV dose is $\geq$ 4200 mg/week. Patients with erythropoietin levels $>$ 500 mU/ml do not respond. Up to 20% of patients on 1200 mg/day ZDV required transfusions. With ZDV 500–600 mg/day, erythropoietin alfa is seldom required.
Granulocytopenia (occurs in up to 50% of AIDS patients)	Ineffective granulopoiesis Antineutrophilic antibodies Drugs: • Zidovudine $\gg$ ddC and ddI • Ganciclovir • Flucytosine • Sulfonamides • Dihydropyridine reductase inhibitors: trimetrexate, pyrimethamine, trimethoprim • Pentamidine • Antineoplastic therapy • Alfa interferon	May respond to granulocyte-colony stimulating factor (G-CSF) or granulocyte-monocyte stimulating factor (GM-CSF). Suggest determining etiology of granulocytopenia and using alternative agents rather than G-CSF or GM-CSF. CSF may be of particular value in antineoplastic chemotherapy regimens during nadir of neutropenia. Use may be associated with Sweet's syndrome and activation of HIV (see Table 6C).
Thrombocytopenia (occurred in 11% in one series, <i>AIDS Res</i> 6:261, 1990)	Early stage HIV-associated thrombocytopenia Drugs: • Antineoplastic therapy • Alfa interferon • Beta-lactam antibiotics • Most other drugs above that cause neutropenia	Clinical: Usually occurs in early HIV infection and platelet counts increase as HIV infection progresses. Studies show $\downarrow$ platelet production and $\downarrow$ platelet survival (<i>Lancet</i> 343:479, 1994). A common epitope demonstrated on HIV p24 and human platelets (<i>Lancet</i> 342:1274, 1993). Pseudothrombocytopenia due to EDTA-induced platelet clumping reported (<i>West J Med</i> 157:668, 1992). Rx: • Treatment may not be necessary; incidence of significant bleeding is low, spontaneous remissions in 10–20%. • In a Swiss study, ZDV therapy increased platelet counts by 50,000 to 100,000/mm³ • IV immune globulin (400 mg/kg qd x 5 days) will usually lead to transient $\uparrow$ in platelet counts, but is expensive. IV anti-D (anti-Rh) antibody: response in 75% (may take 3 weeks) but sustained in $<$ 10%. Not effective in Rh-negative or splenectomized pts (<i>Lancet</i> 2:627, 1986). • Splenectomy: 2/3 of patients will respond if other therapies fail.

Abbreviations: G6PD = glucose-6-phosphate dehydrogenase, INH = isoniazid, TMP/SMX = trimethoprim/sulfamethoxazole

TABLE 7A (20)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Hematologic Abnormalities (<i>continued</i>)		
Thrombotic thrombocytopenia (TTP), hemolytic uremic syndrome (HUS)	TTP and HUS described in HIV+ individuals, etiology unknown	Clinical: Fever, neurologic abnormalities, renal abnormalities, purpura, microangiopathic hemolysis (schistocytes on peripheral smear), thrombocytopenia. Rx: Primary—plasma exchange. Splenectomy, steroids, dextran for salvage rx.
Eosinophilia	Allergic diseases, drug reactions Parasitic infections Non-parasitic infections Neoplasms Skin disorders Pulmonary lymphoid hyperplasia, children	Drugs: Zalcitabine (3–5% pts), ganciclovir ($\leq$ 1% pts), IL-2, other drugs such as TMP/SMX, dapsone. Zidovudine: 2 pts reported with fever, eosinophilia (8, 19%) and cutaneous leukocytoclastic vasculitis after 2–4 weeks of ZDV (<i>Arch Int Med</i> 152:850, 1992). Eosinophilic vasculitis reported before ZDV (<i>Arch Int Med</i> 146:2059, 1986). Parasitic: Strongyloides, Isospora belli (in contrast to cryptosporidia and giardia which are not associated with $\uparrow$ eos). Norwegian scabies. Neoplasms: Hodgkin's disease Skin disorders: Eosinophilic folliculitis (resembles Ofuji's disease); marked pruritus, discrete, erythematous urticarial, follicular papules on trunk, head, neck, proximal extremities. $\uparrow$ eos. $\uparrow$ IgE. CD4 < 250 in 10/13 pts (<i>Mayo Clinic Proc</i> 67:1089, 1992).
Coagulation abnormalities: prolonged partial thromboplastin time (PTT), lupus anticoagulant (present in 20–66% HIV+, <i>Blood Rev</i> 7:121, 1993)		Clinical: An incidental finding in HIV+ patients, not associated with either excessive bleeding or thrombosis in this population. Invasive procedures have been performed without bleeding complications.
Hepatobiliary Disease [Right upper quadrant abdominal pain (discomfort), with or without hepatomegaly, and abnormal liver function tests] [Useful diagnostic tests: • Liver function tests (LFT) ($\uparrow$ transaminase levels in 2–3.8% asymptomatic HIV+ pts) • Ultrasound • CT scan • ERCP • Liver biopsy]	Acalculous cholecystitis AIDS cholangiopathy (sclerosing cholangitis, intra- and extrahepatic) (obstructive biliary tract disease). Etiology is uncertain; the following have been associated: Cryptosporidium Cytomegalovirus Microsporidia Kaposi's sarcoma Mycobacterium avium-intracellulare Lymphoma	Clinical: Prevalence $\uparrow$ in AIDS patients. Right upper quadrant pain, fever in 2/3 but jaundice uncommon (18%). R/O "pseudocholelithiasis" 2° to ceftriaxone, symptomatic in 9% pts with "sludge" in gallbladder by ultrasound. More likely in pts on $\geq$ 2.0 gm/d, on total parenteral nutrition or younger patients on $\geq$ 28 days rx. Lab: Increase in alkaline phosphatase > other LFT abnormalities. Biopsy: In some cases, histologic sections have shown CMV or cryptosporidium. Rx: Appropriate surgical intervention is indicated.
		Clinical: Fever, pain, right upper quadrant tenderness. Median survival of 20 pts was 7 months (<i>Gut</i> 34:116, 1993). Lab: Alkaline phosphatase $\uparrow$ 2–20x normal. Ultrasound or ERCP: Prominent or dilated intrahepatic and/or extrahepatic bile ducts down to periampullary area with marked thickening of ductal walls. Papillary stenosis in 1/2 patients, sphincterotomy may relieve symptoms in these patients. Cryptosporidia or CMV in 9/15 patients (60%) (<i>NEJM</i> 328:95, 1993). Another series (20 pts): cryptosporidia 13, CMV 6. Enterocytozoon bienersi found in 8/8 patients in whom cryptosporidia or CMV not found (<i>NEJM</i> 328:95, 1993).

TABLE 7A (21)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Hepatobiliary Disease (continued)	Hepatic parenchymal disease, see <i>Viral hepatitis</i> , below Etiologies identified in about 40% of patients. Infections: Cytomegalovirus 14%, MAI 11%, <i>C. neoformans</i> 2%, <i>H. capsulatum</i> 1%, <i>M. tuberculosis</i> 1%, <i>C. albicans</i> 0.6%, <i>Penicillium marneffei</i> (see <i>Comments</i>) Neoplasms: Kaposi's sarcoma 9%, non-Hodgkin's lymphoma 1.5%	Clinical: Hepatocellular abnormalities usually reflect systemic infection or malignancy. Histologic findings rarely of diagnostic value. Hepatic histology abnormal in 90% of pts with AIDS: steatosis 42%, portal inflammation 35%, congestion 22%, poorly formed granulomata 14% (<i>Hepatology</i> 7:927, 1987; <i>Am J Med</i> 52:404, 1992). Fever, weight loss, hepatosplenomegaly in pt with travel to Southeast Asia: consider <i>Penicillium marneffei</i> (<i>J AIDS</i> 6:446, 1993).
	Hepatomegaly with severe steatosis, lactic acidosis in patients on antiretroviral therapy	Clinical: Occurs predominantly in women, majority overweight, at least 4 months of anti-retroviral rx (zidovudine, ddI, or ddC). Abdominal pain, hepatomegaly. Lab: Hepatic transaminases 3-10X normal, ↑ triglycerides, ↓ serum HCO ₃ , ↑ arterial ammonia, lactic acidosis, ↑ PTT. Biopsy: severe macrovesicular steatosis. Prevalence: at least 40 cases, mortality > 50%. Incidence < 0.4% (<i>AIDS Clin Care</i> 6:17, 1994).
	Bacillary angiomatosis (peliosis hepatis)	Clinical: Fever, abdominal pain, weight loss, hepato- and splenomegaly. About 1/2 pts will have skin lesions: painful, erythematous plaques or nodules. 1/2 have lymphadenopathy. 2/3 pts give history of cat bite or scratch (<i>JAMA</i> 269:770, 1993). Lab: Alkaline phosphatase ↑ > hepatocellular tests. Etiologic agent related to rickettsia: <i>Bartonella (Rochalimaea) henselae</i> (usual), <i>B. quintana</i> (uncommon). Can be isolated from blood, 5-15 days incubation of lysis-centrifugation cultures on blood agar under CO ₂ (<i>J Clin Micro</i> 30:275, 1992). Rx: Can be rx with erythromycin. Doxycycline and antituberculous drugs may also be effective (<i>NEJM</i> 323:1581, 1990). Patients respond clinically (↓ fever, ↓ symptoms) in 3-4 days, but require up to 2 months for LFTs to become normal. X-ray: May be associated with bone lesions (punched-out appearance). CT/MRI findings: characteristic intrahepatic vascular lakes.
	Drug-associated hepatic dysfunction	Clinical: Multiple drugs used in HIV patients are associated with abnormalities in LFTs; among these are: TMP/SMX (1/2 pts), acyclovir, didanosine (ddI), ZDV, ddC, ganciclovir, foscarnet, ketoconazole, fluconazole, INH, rifampin (see Table 9). Most require dose reduction or discontinuation if abnormalities exceed about 5x normal values.
	Viral hepatitis Hepatitis B (HBV)	Clinical: Risk factors for HIV and hepatitis B are the same (80-90% HIV+ pts are + for HBV markers (<i>Ann Int Med</i> 117:837, 1992). ↑ risk of becoming Hep B chronic carrier (23%). HIV+ pts respond less well to Hep B vaccine and about 1/2 lose antibody after 4 years (<i>NEJM</i> 316:630, 1987; <i>Clin Inf Dis</i> 18:339, 1994).
	Hepatitis C (HCV)	Clinical: HCV infection may be more frequent: Italy 60% HIV+ IDUs, Denmark 4% in HIV+ homosexual men (<i>Am J Med</i> 92:404, 1992). Higher degree of HCV viremia and ↑ rate of HCV antibody loss. Co-infection with HCV and HIV ↑ risk of perinatal transmission of HIV to infant.
	Hepatitis D (delta agent)	Clinical: Antibodies to delta agent in 25% of HIV+, HBV+ individuals. Prolonged antigenemia, ↑ liver injury (<i>Clin Inf Dis</i> 18:339, 1994).

Abbreviations: IDU = injection drug user, MAI = *Mycobacterium avium-intracellulare*

TABLE 7A (22)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Hepatobiliary Disease (continued)	Hepatitis A and E	No data reported
Lung	Most common etiologies are <i>Pneumocystis carinii</i> pneumonia, bacterial pneumonia, tuberculosis	
Cough with normal or minimally abnormal chest x-ray [Useful diagnostic tests: • High resolution CT scan of lung • Pulmonary function tests]	Bronchitis, bronchiectasis	HIV infection/disease not reported to alter the prevalence or course of bronchitis. In pts with chronic productive cough or recurrent pneumonia in same site, consider bronchiectasis. Dx based on CT scan, not evident on chest x-ray in 84% (<i>Quart J Med</i> 85:875, 1992; <i>J Comp Asst</i> Tomo 17:260, 1993). Whether prevalence is ↑ has not been defined.
	<i>Pneumocystis carinii</i> pneumonia	See below
	Emphysema-like bullous disease	On high-resolution CT scan, 42% pts had bullous lesions (<i>Radiol</i> 173:23, 1989). Pulmonary function tests: ↑ residual volume, ↑ functional residual capacity, ↓ diffusing capacity but no airflow obstruction (<i>Ann Int Med</i> 116:124, 1992). Etiology is unknown.
Shortness of breath with abnormal chest x-ray [Useful diagnostic tests: • Arterial blood gases • Expectorated sputum: exam—Gram stain, AFB stain, fungal (KOH) prep; direct fluorescent antibody for <i>Legionella</i> sp.; culture for aerobic bacteria, fungi, mycobacteria • Induced sputum (see Table 20); modified Giemsa stain and direct FA prep (for <i>P. carinii</i> + same studies as with expectorated sputum) • Bronchoscopy with bronchoalveolar lavage; studies as with induced sputum (rarely transbronchial biopsy) • Percutaneous biopsy of lung/mass]	<i>Pneumocystis carinii</i> pneumonia*	CD4 usually < 200/mm ³ Clinical: dry cough, fever, progressive dyspnea Laboratory: arterial blood gas—↓ pO ₂ (< 70 mmHg in 80% patients); pulmonary function tests—restrictive type defect with ↓ vital capacity and ↓ total lung capacity. Diffusion abnormalities common; single breath diffusing capacity for CO < 80% of predicted (90% sensitivity but only 25% specificity). Chest x-ray:** 5–10% have normal chest x-ray (in these pts, CO diffusing capacity, ↓ PaO ₂ with exercise may be of particular value). Most common: diffuse bilateral symmetrical fine heterogeneous reticular infiltrates Less common: Unilateral/focal distribution of same quality infiltrates or focal alveolar consolidation (especially upper lobe in patients on aerosolized pentamidine prophylaxis) or an interstitial pattern with fine nodular infiltrates or miliary lesions or focal nodules without cavitation, thick-walled cysts or pneumatoceles or pneumothorax Rare: pleural effusion and/or intrathoracic adenopathy After 4 days of treatment with trimethoprim/sulfamethoxazole, there is commonly an ↑ infiltrate resembling pulmonary edema. This complication is significantly reduced when corticosteroid rx used with TMP/SMX in patients with low pO ₂ (see Table 8, page 70). Response: with effective rx, improvement is expected in 7–10 days. Sputum, induced: detection of <i>P. carinii</i> —sensitivity 77%, negative predictive value 64%; use of fluorescent antibody technique markedly improves detection over that with Giemsa stain. Bronchoalveolar lavage (BAL): Do not delay initiation of rx if BAL not immediately available. Treatment for several days does not ↓ diagnostic sensitivity. Detection of <i>P. carinii</i> —sensitivity 85–99%. Transbronchial biopsy: detection of <i>P. carinii</i> —sensitivity 88–97%. <i>P. carinii</i> rarely found on transbronchial biopsy if not found on BAL.

* Adapted from P.C. Hopewell, H. Masur, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994. ** Adapted from P.C. Goodman, *ibid*.
Abbreviations: BAL = bronchoalveolar lavage

TABLE 7A (23)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Lung (continued) Shortness of breath with abnormal chest x-ray (continued)	Toxoplasma gondii pneumonia	Clinical: Rare in U.S., in France represents up to 5% of cases of suspected PCP. 6 cases reported, CD4 < 100/mm ³ in 4 of 5 (<i>Arch Int Med</i> 152:1073, 1992). 2 pts on aerosolized pentamidine, 4 on no PCP prophylaxis. Febrile illness, minimal cough, ↑ dyspnea. Chest x-ray: Diffuse interstitial or diffuse coarse nodular (resembles PCP). Pleural effusion in 2/6 patients. Lab: ↑ transaminase, ↑ LDH. Sputum: BAL + for T. gondii.
	Histoplasmosis (<i>Histoplasma capsulatum</i>)	A common reactivation infection when CD4 < 200/mm ³ in pts with geographical history of having been in the "histo belts" (Ohio-Mississippi River Valley, southeastern U.S., St. Lawrence River Valley, Central America and northern South America). Clinical: Usually presents with nonspecific systemic complaints: fever, weight loss, night sweats, but lungs commonly involved with shortness of breath. Hepatosplenomegaly and rarely focal cutaneous pustules or ulcers may be presenting findings. Pts may also present with "septic shock" including DIC. X-ray: Commonly shows diffuse, bilateral poorly defined small (1–2 mm) nodular infiltrates with or without hilar/mediastinal adenopathy. Dx: Identification of H. capsulatum in WBC on peripheral blood smear or bone marrow (PAS or silver stain) and culture (about 90% are positive). If suspected and blood/bone marrow not positive, biopsy lymph node, liver, lung or lesions. About 80% will have positive immunodiffusion or complement fixation test for antibodies.
	Coccidioidomycosis (<i>Coccidioides immitis</i>)	A common reactivation or primary infection in patients from "cocci belt" (southwest U.S.) with CD4 < 150/mm ³ . In HIV-negative individuals, annual incidence of symptomatic infection is 0.43%, in HIV+ individuals 25% developed symptomatic cocci over 41 months (<i>Am J Med</i> 94:235, 1993). Cases of cocci have ↑ 10x in central California valleys in 1992 vs 1990 (<i>MMWR</i> 42:21, 1993). 15% pts had simultaneous PCP (<i>Med</i> 69:384, 1990). Clinical: Presentation is similar to histoplasmosis, severe shortness of breath is common. X-ray: Diffuse bilateral reticulonodular infiltrate similar to histoplasmosis. Distinctly nodular pattern unusual with PCP. Dx: While complement fixation antibody tests are frequently positive, dx is established by identification of large spherules of C. immitis directly or on culture.
	Lymphocytic interstitial pneumonia (LIP)	A disease of unknown etiology which may present with shortness of breath in children with HIV infection (see Table 12D, page 89). X-ray: Resembles PCP with diffuse or focal, fine to medium reticular interstitial infiltrate. Findings gradually worsen over months. Dx: Lung biopsy is necessary for dx; shows an accumulation of lymphocytes and plasma cells in interstitial areas. Rx: Corticosteroids may be beneficial.
	Primary pulmonary hypertension	30 cases reported. Clinical: dyspnea, right-sided heart failure. Lung biopsies show plexogenic lesions. Etiology is undetermined (<i>S Med J</i> 87:357, 1994).

Abbreviations: DIC = disseminated intravascular coagulopathy, PAS = periodic acid Schiff stain

TABLE 7A (24)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Lung (continued) Shortness of breath with abnormal chest x-ray (continued)	Pulmonary eosinophilia (Loeffler's syndrome)	Can be caused by drugs commonly used in HIV+ pts: sulfonamides, dapsone, penicillin (Lancet 343:860, 1994).
	Ehrlichiosis (Ehrlichia chaffeensis)	A case report, pt presented with fever, tachypnea, neutropenia with 17% bands, thrombocytopenia, ↑ hepatic enzymes. Chest x-ray: diffuse bilateral infiltrates. Arterial blood gases: ↓ PaO ₂ . Patient deteriorated. Diagnosis suspected on last day, optimal antibiotic rx not given (NEJM 329:1164, 1993).
	Congestive heart failure	See Heart
Fever, cough with abnormal chest x-ray	Mycobacteria:	
	Tuberculosis (Mycobacterium tuberculosis*)	Tuberculosis often occurs before pt has AIDS defining illness. Most cases due to reactivation but primary tuberculosis being recognized with increasing frequency. 10% of HIV+ individuals are tuberculin +, in U.S. ~4% AIDS pts have had TB, in Italy 11% (J Infect 28:261, 1994). Rate of development of TB is 8%/year. Average CD4 count is 375/mm³. Clinical presentation varies with stage of HIV infection: Early HIV infection (CD4 > 400/mm³): Reactivation. Typical presentation with upper lobe cavity disease most common. Extrapulmonary disease uncommon. PPD (5 TU) is + (≥ 5 mm induration) in 80%. Later HIV infection (CD4 < 400/mm³): Either reactivation or progressive primary disease (30–50%). Clinical: Fever, cough (may be absent), shortness of breath, weight loss, night sweats. ½ to ¾ involve extrapulmonary sites, especially lymph nodes and bone marrow (granulomas in 50% of bone marrow biopsies). Mycobacterial blood cultures + in ¼ to ½ of patients. (BACTEC system is sensitive and rapid.) Caution: patients reported with blood + for both M. tbc and MAI. Cultures of urine, joint fluid, CSF, liver, GI mucosa and ascites may also be +. Mass lesions of brain (tuberculoma) may mimic CNS toxoplasmosis. PPD (5 TU) positive (≥ 5 mm induration in < 25% with clinical AIDS). X-ray: Mediastinal-hilar adenopathy most common with progression to diffuse, somewhat coarse interstitial densities or localized infiltrates, especially in mid or lower lung fields. Pleural effusion in 10–20%. Disseminated (reticulonodular infiltrates, not classic "miliary" since "millet" are granulomata, not seen in HIV with low CD4) the most common with CD4 < 200/mm³. Hilar/peritracheal adenopathy uncommon with PCP or bacterial pneumonia, common in TB. Sputum: Smears positive for AFB in 40–50% pts with pulmonary TB, BAL + in 50–60%, culture + in 80–90%.

Multidrug Resistant (MDR) Tuberculosis. **ANY PT SUSPECTED OF TB SHOULD BE ISOLATED** [private room, negative pressure, health care workers (HCW) and visitors entering should wear high efficiency disposable masks] [for details: MMWR 39(RR-17):14, 1990]. By September 1992 clusters of MDR TB reported in 14 U.S. hospitals and 1 prison system (Ann Int Med 118:77, 1993). Some organisms resistant to 7 drugs (INH, RIF, KM, ETB, ethionamide, SM, rifabutin). Nosocomial transmission in 7 hospitals and prison. MDR TB diagnosed in 241 pts, 17 HCW. Most transmission among AIDS pts. Acquisition of MDR reported in HIV+ pts being treated for sensitive M. tbc (NEJM 328:1137, 1993). Interval between exposure and diagnosis 1–3½ months, diagnosis to death 4–16 weeks, mortality 72–89%. TBn skin test conversions in 18–50% HCW. 1 HIV neg. HCW has died (MMWR 41(RR-11):52, 1992).

* Adapted from P.C. Hopewell, Medical Management of AIDS, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994.

Abbreviations: M. tbc = Mycobacterium tuberculosis; TBn = tuberculin; INH = isoniazid; RIF = rifampin; KM = kanamycin; ETB = ethambutol; SM = streptomycin

TABLE 7A (25)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Lung (continued) Fever, cough with abnormal chest x-ray (continued)	<i>Mycobacteria (continued)</i> Infection due to <i>Mycobacterium avium</i> -intracellular complex [Mycobacterium genavense, an unrelated organism which clinically behaves like MAI, antibiotic susceptibilities not known (Clin Inf Dis 18:455, 1994)] Infection due to <i>Mycobacterium kansasii</i> Community-acquired pneumonia Bacterial (Am J Epidemiol 138:909, 1993): Streptococcus pneumoniae 35-70% Haemophilus influenzae 3-40% Staphylococcus aureus 7% E. coli 6-7% Other Gram-negative 7-9% Prevalence not defined: Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella sp. Nosocomial-acquired pneumonia Bacterial: aerobic Gram-negative bacilli, Legionella pneumophila Cryptococcosis (Cryptococcus neoformans)	Clinical: CD4 usually $\leq 50/\text{mm}^3$ (see Table 4). Usually presents as disseminated infection with symptoms of fever, weight loss, night sweats, diarrhea, anemia and neutropenia, but may be asymptomatic even with positive blood cultures. Lab: Colonization of respiratory secretions and GI tract is common and may precede disseminated disease. When symptomatic, blood cultures are usually positive for MAI (BACTEC system is very sensitive). Dual infection with M. tuberculosis recognized. X-ray: When lungs involved, heterogeneous interstitial infiltrates with or without hilar lymphadenopathy. X-ray: Infiltrates "atypical"; alveolar, interstitial or diffuse parenchymal or pleural effusion. Upper lobe cavities uncommon. 1/2 have extrapulmonary dissemination (Rev Inf Dis 13:789, 1991). Pneumococcal pneumonia is common in HIV+ patients (86% S. pneumo serotypes isolated included in pneumococcal vaccine, Table 13). Annual incidence of invasive disease due to S. pneumoniae is 1100 per 100,000 men with AIDS, age 25-44 years (JAMA 265:3275, 1991). Clinical: Typical presentation with fever, chills, productive cough, pleuritic chest pain and dyspnea can be seen at all stages of HIV infection. Most (up to 85%) of HIV+ patients with pneumococcal pneumonia will have positive blood cultures. X-ray: Usually consolidation (homogeneous densities) with either segmental or lobar distribution. Course: Response to appropriate antibiotics is usually prompt (48-96 hours to become afebrile, radiographic resolution is much slower, as it is in non-HIV+ patients). If patient fails to respond as above, consider concomitant PCP or TB. Haemophilus influenzae pneumonia/bacteremia : occurs with ↑ frequency. Incidence of invasive disease is 80/100,000. In one series, most pts had pneumonia, in another only 30% had pneumonia. 1/2-1/2 isolates are type b, 15/15 reported were β-lactamase negative. Response to appropriate antibiotics is prompt. Role of immunization against Hib can be questioned, incidence of disease ↑ but not striking, only 1/2-1/2 are type b but HIV+ pts respond to vaccine (NEJM 325:1837, 1991) (See Table 13). HIV infection/disease not reported to alter the prevalence or course of nosocomial, usually ventilator-acquired, Gram-negative bacillary pneumonia. Nosocomial Legionella pneumophila pneumonia uncommon but reported in several small series (Clin Inf Dis 18:227, 1994). M. avium may be acquired from hot water systems (Lancet 343:1137, 1994). C. neoformans is a ubiquitous soil fungus which usually affects the CNS (see Meningitis) in patients with CD4 < 100/mm ³ . Site of entry is usually the lungs and pneumonia has been reported. X-ray: Variable pattern; single or multiple well-defined nodules with or without cavitation or diffuse reticular infiltrates and/or hilar/mediastinal adenopathy. Occasionally a reticulo-nodular pattern may occur. Dx: Isolation of C. neoformans from respiratory secretions. Serum CRAG may be positive.

Abbreviation: PCP = Pneumocystis carinii pneumonia

TABLE 7A (26)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Lung (continued) Fever, cough with abnormal chest x-ray (continued)	Aspergillosis	Aspergillus sp. are commonly isolated from respiratory sites (4%), but invasive aspergillosis developed in only 15% of colonized patients, more common in pts with AIDS and associated neutropenia (<i>Clin Inf Dis</i> 14:141, 1992). Clinical: 33 patients reported in one series. 64% had an episode of infectious pneumonia $\leq$ 1 year before. CD4 $<$ 50/mm ³ . All were febrile, cough 97%, dyspnea 80%, chest pain 20%, hemoptysis 17%. 21% CNS signs. Chest x-ray: cavities 42% (most upper lobe), bilateral interstitial infiltrates 54%, pleural effusion 15%. Despite rx, mean time to death was 8 weeks (<i>Am J Med</i> 95:177, 1993).
	Blastomycosis	Uncommon, largest series is 15 cases (<i>Ann Int Med</i> 116:847, 1992). CD4 $<$ 200/mm ³ . Pulmonary (7 cases): 4 dyspnea, 2 chest pain, chest x-ray 3 local, 3 diffuse reticulo-nodular. BAL cultures +. Disseminated (8 cases): CNS involvement (5 cases), multiple organs (6 cases).
	Nocardiosis (<i>Nocardia asteroides</i>)	Uncommon, 43 cases reported (<i>Med</i> 71:128, 1992). CD4 $<$ 200/mm ³ . Clinical: Fever, malaise, cough, weight loss. Chest x-ray: 83% abnormal, cavitation 62%, lobar consolidation 52%, pleural effusion 33%, reticulonodular infiltrates 33%. Lab: Blood cultures rarely +.
	Viral pneumonia Cytomegalovirus (CMV)	The importance of CMV pneumonitis in HIV+ pts is controversial. 90% of AIDS pts have evidence of CMV at autopsy. Viral cultures of BAL fluid are frequently positive. CMV has been isolated from 30% of pts with PCP, and associated with $\uparrow$ mortality (<i>Am J Med</i> 78:429, 1985), but rx with ganciclovir does not appear to affect outcome (<i>NEJM</i> 314:801, 1986). Would rx if biopsy revealed interstitial inflammation with CMV inclusions and no other pathogens.
	Influenza virus	HIV+ not associated with $\uparrow$ susceptibility to influenza. Amantadine prophylaxis will protect vs influenza A (<i>JAMA</i> 261:245, 1989). Immunization recommended, although pts with AIDS have $\downarrow$ response (<i>Ann Int Med</i> 109:383, 1988).
	Measles	In U.S., 9 of 11 patients had pneumonitis; 3 had no rash and 8 had atypical exanthems; mortality 3/11 (<i>JAMA</i> 267:1237, 1992). Immunization of HIV+ children recommended, although immune responses may be $\downarrow$. Ribavirin aerosol has been used but efficacy not proven (<i>ibid.</i>).
	Adenovirus	Based on lack of reports, no apparent $\uparrow$ in susceptibility. Adenovirus diarrhea important (see page 34).
	Human herpesvirus 6 (HHV-6)	HHV-6 infected cells detected in tissues obtained at necropsy in 9/9 pts. In one pt, probably primary cause of fatal pneumonitis. Relevance is that HHV-6 infections may be treatable with ganciclovir and foscarnet (<i>Lancet</i> 343:577, 1994).

TABLE 7A (27)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Lung (continued) Fever, cough with abnormal chest x-ray (continued)	Kaposi's sarcoma (KS)*	Clinical: Usually but not always associated with cutaneous and/or mucosal KS. May present with cough, bronchospasm and shortness of breath. X-ray: Findings are somewhat distinctive: coarse, poorly defined nodular densities throughout the lungs with concomitant coarse linear densities in the perihilar regions. Nodules increase slowly in size, rapid ↑ suggests hemorrhage. Pleural effusions common (up to 50%). Hilar adenopathy rare (< 10%). Dx: Bronchoscopy will usually show typical violaceous endobronchial lesions.
	Lymphoma	Lymphomas associated with advanced HIV infection are becoming increasingly common, are usually non-Hodgkin's B cell type, with extranodal involvement the rule. Thoracic involvement is uncommon (10%) but when it occurs produces pleural effusion in 50%, hilar and/or mediastinal adenopathy in ¼ and either reticulonodular interstitial infiltrates or alveolar consolidation in 25%.
Mass lesion ± necrosis (abscess)	All of the entities above with abnormal chest x-ray Rhodococcus equi Mycobacterium tuberculosis Pneumocystis carinii	One-half of pts with Rhodococcus equi present with slowly progressive mass lesion which cavitates (<i>Rev Inf Dis</i> 13:91, 1991). Has tendency to relapse, may require surgery and long-term suppressive rx.
Hilar and/or mediastinal adenopathy	Mycobacterium tuberculosis Mycobacterium avium-Intracellulare Fungal: Histoplasmosis, coccidioidomycosis, cryptococcosis, blastomycosis Lymphoma	See above
Pleural effusion	Infections (66%): Bacterial pneumonia 31% P. carinii pneumonia 15% M. tuberculosis 8% Others (each < 5%): Septic embolism, N. asteroides, C. neoformans, MAI Non-infectious (31%): Hypoalbuminemia 19% Heart failure 5% Others: Kaposi's sarcoma, atelectasis, uremia, ARDS	Incidence in 222 pts was 27% (<i>Ann Int Med</i> 118:856, 1993). Large effusions associated with Kaposi's sarcoma, tuberculosis and lymphoma.
Pneumothorax	P. carinii pneumonia + aerosolized pentamidine	Occurred in 2% of a large series of patients (<i>Ann Int Med</i> 114:455, 1991).
Musculoskeletal System Pyomyositis (Useful diagnostic tests: • Aspiration of lesions: stains, cultures, histopathology of materials • CT or MRI scans)	Pyomyositis: staphylococcal; aerobic gram-negative bacilli (uncommon)	Clinical: May follow exercise, local trauma or injections. Swelling in muscular area, localized pain and fever. ESR usually ↑. Erythema often absent, can be indolent. WBC may be normal and blood cultures usually negative (<i>Am J Med</i> 90:595, 1991).

* Adapted from L.D. Kaplan, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994.

Abbreviations: ESR = erythrocyte sedimentation rate, ARDS = adult respiratory distress syndrome

TABLE 7A (28)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Musculoskeletal System (<i>continued</i>) Arthritis, polyarticular [Useful diagnostic tests: • Aspiration of synovial fluid: WBC count, culture, glucose]	Reiter's syndrome: urethritis or cervicitis, conjunctivitis, arthritis, and mucocutaneous lesions (circinate balanitis, keratoderma blennorrhagica)	Clinical: Reiter's syndrome occurs in 0.5–10% of HIV+ patients, 75% are HLA B-27 positive (<i>Rheumatol Int</i> 9:137, 1989). Typically, non-bacterial urethritis 7–14 days after sexual exposure. Asymmetric polyarticular arthritis involving large joints of legs, including toes, develops over several weeks. Mucocutaneous lesions include circinate balanitis and keratoderma blennorrhagica. Typically resolves in 3–4 months but ~50% have recurrences. Lab: Synovial fluid typically is translucent, 2000–100,000 cells/ μ l, > 50% PMNs, culture negative, glucose < 50 mg/dl lower than blood glucose. Rx: Since often associated with C. trachomatis, empirical rx for chlamydia (<i>see Table 8</i>) is appropriate. In non-HIV+ patients, methotrexate or folic acid antagonists have been used; they should not be used in HIV+ patients.
	Psoriatic arthritis	Clinical: Psoriasis noted in 1–5% HIV+ population. Frequency of arthritis $\uparrow$ in HIV+ pts with psoriasis (<i>Rheum Dis Clin NA</i> 17:59, 1991).
	"Lightning pain" syndrome	Severely painful acute attack of arthralgia or myalgia, lasts a few hours to a few days. Often requires narcotics for relief. Clinical exam normal. Cause unknown, no sequelae (<i>Med J Aust</i> 158:114, 1993).
	Rheumatoid arthritis	Virtually never occurs in pts with HIV. Several pts with seropositive RA have gone into remission after infection with HIV.
Arthritis, oligoarticular	HIV-associated arthritis	Usually asymmetrical, lower limbs. HLA B27 negative. Synovial fluid: low WBC with PMNs (<i>Med J Aust</i> 158:114, 1993).
Myopathy (progressive proximal muscle weakness) [Useful diagnostic tests: • CPK • EMG]	HIV-1 associated myopathy	Clinical: Proximal muscle weakness, $\uparrow$ creatinine kinase levels. Muscle biopsy: $\frac{1}{2}$ had inflammatory infiltrates. $\frac{1}{2}$ pts rx with and responded to prednisone (<i>Ann Int Med</i> 113:492, 1990).
	Drug-associated: zidovudine (ZDV)	Clinical: Proximal muscle weakness and atrophy (legs > arms, "saggy butt" syndrome) occurred in 5/86 pts (6%) rx with ZDV > 6 months (mean 45 weeks). Creatinine kinase $\uparrow$ (average 777 u/L). Muscle biopsy: "Ragged red fibers" on histology, abnormal mitochondria on EM. Improves with discontinuation of ZDV, recurs with rechallenge (<i>Ann Int Med</i> 113:492, 1990). ddC also causes a selective loss of mitochondrial DNA in vitro (<i>Lancet</i> 337:508, 1991).
	Polymyositis	A dermatomyositis-like disease has been described in AIDS (<i>Rheum Dis Clin NA</i> 17:117, 1991).
Pancreatitis (hyperamylasemia with or without abdominal pain) [Useful diagnostic tests: • Serum amylase • X-ray: Flat film of abdomen. Ultrasound or CT scan of upper abdomen]	Drug-associated pancreatitis	Clinical: On recommended doses, 5–9% of patients on didanosine (ddi) will develop pancreatitis ($\uparrow$ amylase, abdominal pain). Fatal in 0.35% patients. In pts with history of pancreatitis, 8/27 pts on ddi developed pancreatitis. Pancreatitis occurs in < 1% on ddC. In patients with a history of pancreatitis on ddC, 3.2% developed pancreatitis or $\uparrow$ amylase. IV pentamidine is associated with pancreatic islet cell damage (hypoglycemia with later diabetes mellitus). It is rare but reported after long-term aerosolized pentamidine (<i>Am J Med</i> 88:53N, 1990).

Abbreviations: CPK = creatinine phosphokinase, EMG = electromyogram

TABLE 7A (29)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Peritoneal Disease [Useful diagnostic tests: Paracentesis—protein, cell count, cytology, bacterial culture, AFB stain & culture, viral culture; laparoscopic evaluation—biopsy implants if seen] Ascites, sudden onset Transudative ascitic fluid (< 3 gm protein/100 ml)	Concomitant hepatic cirrhosis (alcoholic), congestive heart failure, inferior vena cava obstruction, Budd-Chiari syndrome, hypoalbuminemia, vasculitis	Clinical: Symptoms and signs of underlying process.
Exudative ascitic fluid (> 3 gm protein/100 ml) (> 500 cells/mm suggests infection, neoplasm)	Tuberculosis, lymphoma, cytomegalovirus	Clinical: Collect large volume (500–1000 ml), centrifuge; may reveal AFB on smear Biopsy: Etiology most often found on biopsy.
Renal Proteinuria and azotemia [Useful diagnostic test: renal biopsy]	HIV-associated glomerulosclerosis	Clinical: 65% pts are black. Massive proteinuria of sudden onset, hypoalbuminemia, renal insufficiency rapidly progressing to endstage renal disease. Peripheral edema and hypertension minimal or absent. Renal biopsy: Focal glomerulosclerosis with mesangial deposits of C3, IgM. Course: Death in 3–6 months even with dialysis. Some reports suggest that ZDV may ↓ proteinuria and improve renal function (<i>Ann Int Med</i> 112:35, 1990).
	HIV-associated IgA nephropathy	Clinical: Rarer than HIV glomerulosclerosis. All reported pts are white. Microscopic hematuria, minimal proteinuria. ↑ serum IgA. Progression of disease is slow. Thought to be immune complex disease (<i>NEJM</i> 327:702, 1992).
	Amyloidosis	Clinical: Very rare [1 case report with nephrotic syndrome (<i>Clin Inf Dis</i> 14:189, 1992)].
	Heroin nephropathy Nephrotoxic drugs: pentamidine, foscarnet, aminoglycosides, amphotericin B	
*Sepsis/Bacteremia	Disseminated pneumococcal disease	Clinical: 30–50% of pts with pneumococcal pneumonia have bacteremia. Rate of <i>S. pneumoniae</i> bacteremia is 100-fold ↑ in HIV+ patients. It often occurs in early stage HIV disease. 86% of serotypes are included in current vaccine (<i>Am J Epidemiol</i> 138:909, 1993). Outcome of rx has been good, although rare relapsing infections reported (<i>Clin Inf Dis</i> 14:1050, 1992). In addition, <i>S. pneumoniae</i> may cause soft tissue infections (<i>J Inf Dis</i> 163:897, 1991) (See page 45).
	<i>Haemophilus influenzae</i> bacteremia	See page 45
	Etiologies include those seen in the non-HIV+ patient, especially the febrile neutropenic patient: enterobacteriaceae, <i>Pseudomonas</i> sp., <i>Staph. aureus</i> , <i>Staph. epidermidis</i>	Nasopharyngeal carriage rates for <i>Staph. aureus</i> in HIV+ 44% vs 23% in hospital personnel; rates of <i>Staph aureus</i> bacteremia ↑ (<i>Europ J Clin Micro-ID</i> 11:985, 1992).
Recurrent bacteremia	Non-typhi salmonella, especially <i>S. typhimurium</i> (outside of U.S., <i>Salmonella typhi</i>)	In U.S., 20-fold ↑ in risk in HIV+ individuals (<i>Rev Inf Dis</i> 9:925, 1987). With CD4 > 200/mm ³ clinical presentation and response to rx similar to HIV-negative individuals. With CD4 < 200/mm ³ , diarrhea is a less prominent symptom. 1–16% relapse within several months (<i>Arch Int Med</i> 151:381, 1991). ZDV (≥400 mg/day) may be effective in preventing recurrences (<i>J Inf Dis</i> 163:415, 1991).
	<i>Mycobacterium avium-intracellulare</i> (MAI)	See page 45
	<i>Bartonella (Rochalimaea) henselae</i>	See page 41

TABLE 7A (30)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Sinuses, paranasal [Useful diagnostic tests: • CT scan • Paracentesis, early for culture]	Sinusitis: microbial flora similar to HIV-negative (<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>B. catarrhalis</i>) plus other Gram-positives (<i>Staph. epidermidis</i> , <i>P. acnes</i>), aerobic Gram-negatives (<i>Pseudomonas aeruginosa</i>), fungi (<i>aspergillus</i> , <i>rhizopus</i> (<i>mucor</i>), <i>Alternaria alternata</i>)	Clinical: Sinusitis occurs in 1/3 to 2/3 of adults with AIDS (<i>Ear, Nose, Throat J</i> 69:460, 1990). Sinusitis may be part of acquired atopy in AIDS (<i>J Inf Dis</i> 167:283, 1993). 1/3 pts are symptomatic (fever, nasal congestion, discharge). X-ray: 79% had air fluid level, usually more than one sinus. Despite rx, 60% pts had recurrent or persistent infection (<i>Am J Med</i> 93:163, 1992). Antral puncture required for accurate cultures and indicated if rx against common pathogens fails (<i>Clin Inf Dis</i> 16:404, 1993).
Skin/Hair* Maculopapular lesions	Acute (seroconversion) HIV disease Molluscum contagiosum Syphilis Candidiasis Cryptococcosis Histoplasmosis Mycobacterial infections: <i>M. tuberculosis</i> , <i>M. avium-intracellulare</i> , <i>M. kansasii</i> , <i>M. marinum</i> , <i>M. hemophilum</i> Mycobacterium leprae Penicillium marneffei Cutaneous Pneumocystis carinii Human papillomavirus (warts, condyloma acuminatum) Drugs Insect bites (scabies—axilla, groin, fingerweb; fleas—lower legs; mosquitoes—arms and legs) Kaposi's sarcoma	Lesions 5–10 mm diameter, symmetrical, especially on face or trunk (may involve palms and soles), erythematous, non-pruritic. Constitutional "mono-like symptoms:" fever (87%), skin rash (68%). Mean duration of symptoms/signs 21 days (<i>Clin Inf Dis</i> 17:59, 1993). Occurs in 8–15% AIDS pts. 2–5 mm pearly flesh-colored papules, often with central umbilication on face, anogenital region. <i>See Genital Tract, page 36</i> Children: diaper-rash type rash involving trunk and extremities. Adults: red, hemorrhagic maculopapular lesions. Common. Widespread skin-colored, dome-shaped translucent papules 1–4 mm in diameter. Resemble Molluscum contagiosum. Slightly pink 2–6 mm cutaneous papules to larger reddish plaques and multiple shallow crusted ulcerations. Vary from acneiform plaques, pustules or indurated verrucous plaques to ulcerative nodular lesions. Clinical presentation of borderline leprosy similar in HIV+ and HIV–, but rx for neuritis less successful in HIV+ (<i>Lep Rev</i> 63:134, 1992). Clinically present with fever, weight loss, small maculopapular skin lesions (2/3 pts), hepatosplenomegaly, adenopathy. Almost all lived or traveled in Southeast Asia (<i>J AIDS</i> 6:466, 1993; <i>Clin Inf Dis</i> 15:744, 1992). Rare but reported with underlying PCP. More common if pt on aerosolized pentamidine. Typically verrucous translucent papules anywhere on body. Diffuse flat and filiform lesions, often in unusual sites. <i>See GI and Genital Tract, above.</i> HIV+ pts have ↑ frequency of skin reactions to most drugs. Erythematous, urticarial papules. Early lesions are round or irregular pinkish-red to violaceous macules to papules. Often symmetrical along skin tension lines.

* Adapted from T.C. Berger, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994; and M.J. Zalla, W.P. Daniel, Sr. and A.F. Fransway, *Mayo Clin. Proc.* 67:1089, 1992.

TABLE 7A (31)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Skin/Hair (continued)		
Nodular, verrucous, and/or ulcerative lesions	Mycobacterial infections Bacillary angiomatosis Acanthamoeba, disseminated Sporotrichosis Cryptococcosis Histoplasmosis Kaposi's sarcoma Non-Hodgkin's lymphoma	See above Friable vascular papules, cellulitis, plaques and subcutaneous nodules, usually tender. Etiology: Bartonella (Rochalimaea) henselae and B. quintana. May be isolated from blood (5–15 days incubation of lysis centrifugation cultures on blood agar, 5% CO₂) and identified with Warthin Stary stain. See <i>Liver</i>, above. Rare, but have seen several cases. Uncommon, but reported Lesions usually not tender Skin involved in 15% of pts with non-Hodgkin's lymphoma. Lesions are usually papules or nodules.
Vesicular bullous or pustular lesions	Herpes simplex virus Varicella-zoster virus Cytomegalovirus Staphylococcal impetigo "Typical scabies" Porphyria cutanea tarda	Grouped vesicles on erythematous base, rapidly evolve into ulcerations or fissures. May persist as chronic large ulcerative lesions. Grouped vesicles on erythematous base. May be verrucous. In chronic form may persist as hyperkeratotic lesions. Dermatomal distribution. Small reddish-purple macules that ulcerate. May present with non-healing perianal ulceration. Erythematous crusted papules, may be pruritic on face, trunk, groin. Extremely pruritic, papular and vesicular lesions characterized by linear or serpentine burrows most commonly on hands, wrists, elbows, ankles. Average number of mites is 11. Association with HIV described. Lesions especially over sun-exposed areas.
Papulosquamous lesions	Seborrheic dermatitis Xerotic eczema (dry-skin syndrome) Dermatophytosis Tinea versicolor Psoriasis Crusted (Norwegian) scabies	Occurs in 20–80% HIV+ individuals, dandruff to patches and plaques of erythema with indistinct margins and yellowish scale on "hairy" areas. Occurs in 5–20% HIV+ individuals. Often severely pruritic and resistant to antihistamines. Occurs in 20% HIV+ individuals. Widespread, often severe with scaly red pruritic papules and plaques. Patchy areas of fine scale and hypopigmentation. CD4 often > 300/mm³. Usually resistant to topical agents. Occurs in 1.3–5% HIV+ individuals. Presents as (1) discrete plaques or (2) a diffuse dermatitis often associated with palmoplantar keratoderma. Distribution may be atypical: groin, axilla and scalp rather than elbows and knees. Characterized by erythema, hyperkeratosis and crusting. Pruritus is typically absent but in AIDS pts pruritus commonly occurs. Burrows usually not seen. Gross nail thickening and subungual debris common. Alopecia, hyperpigmentation, pyoderma and eosinophilia may occur. Dx is based on demonstration of heavy mite burden (1000s).

TABLE 7A (32)

CLINICAL SYNDROME	MAJOR DIAGNOSTIC CONSIDERATIONS	DIAGNOSTIC CLUES/COMMENTS
Skin/Hair (<i>continued</i>)		
Folliculitis	Staphylococcal folliculitis Eosinophilic folliculitis	An uncommon presentation is violaceous plaques (up to 10 cm) in groin, axilla and scalp. See <i>Hematologic Abnormalities, eosinophilia, page 40</i>
Hair disease	Diffuse thinning Premature greying Elongated eyelashes	
Nail disease	Onychomycosis Longitudinal pigmented nail bands	Seen in almost 1/2 pts on ZDV, more common in dark-skinned patients, occurs within 4-8 weeks of starting rx.
Systemic, wasting syndromes	"Slim" disease (enteropathic AIDS), rule out: Cryptosporidium and other causes of chronic diarrhea Mycobacterium avium-intracellulare Mycobacterium tuberculosis Histoplasma capsulatum Kaposi's sarcoma Non-Hodgkin's lymphoma	Weight loss is common (29%) in one series in U.K. Causes: opportunistic infections (47%), psychosocial factors (17%), drug-related problems (7%), unexplained (29%) (<i>Int J STD & AIDS</i> 4:234, 1993). In Africa, the most common symptom in AIDS patients is diarrhea (40-80% of patients). Profound weight loss (may be > 30% of body weight), persistent diarrhea, chronic fever has been called enteropathic AIDS or "slim" disease. The diarrhea is intermittent, watery, without mucus or blood. 1/4 to 1/2 have parasites, most commonly cryptosporidium and Isospora belli. Many patients die from wasting without an apparent opportunistic infection. Treatment regimens have been unfeasible and/or unsuccessful. Dronabinol (Marinol) (a synthetic form of tetrahydrocannabinol) (2.5 mg bid) has been shown significantly to ↑ appetite in AIDS patients and is FDA-approved for this indication. Megestrol acetate (Megace), a synthetic derivative of progesterone, also has recently been approved by the FDA for treatment of anorexia, cachexia or unexplained sudden weight loss in AIDS patients. See Table 6D, page 20. Pentoxifylline has not benefited pts with AIDS-wasting (<i>Clin Inf Dis</i> 18:97, 1994).

TABLE 7B
NEUROPSYCHIATRIC SYNDROMES: DIAGNOSTIC FEATURES*

SYNDROME	DIAGNOSTIC FEATURES/COMMENTS
Depression, major	Occurs in 4-14% HIV+ individuals vs 5% in general population. Many of the symptoms are also symptoms of HIV disease: forgetfulness, loss of interest in work, ↓ libido, blunted affect, withdrawal, poor concentration. When in doubt, consider as depression and treat. Medications which can cause depression include: zidovudine, ddI, acyclovir, corticosteroids, dapsone, pyrimethamine, sulfonamides, TMP/SMX, INH. Exclude CNS opportunistic infections, uncommon if CD4 > 200/mm ³ . Diagnosis of depression requires at least 5 of the following 9 symptoms, including number 1 or 2 within a 2-week period: 1. Depressed mood, 2. markedly diminished pleasure in all activities, 3. significant unintentional weight loss or gain, 4. insomnia or oversleeping, 5. fidgetiness, slowed movement or speech slowing, 6. fatigue or loss of energy, 7. feelings of worthlessness or excessive inappropriate guilt, 8. ↓ ability to think or concentrate, 9. recurrent suicidal thoughts.
Dementia/organic brain disease	70% of pts will experience organic brain disease during course of illness, 2/3 will be moderate to severe. Symptoms include psychomotor agitation, impaired social or occupational functioning, impaired judgment, personality changes. See page 21.
Anxiety/panic disorder	Symptoms include trouble falling asleep, impaired concentration, psychomotor agitation, fatigue. Medications which can cause anxiety include ddI, ganciclovir, sulfonamides. Occurrence of discrete episodes with "fight or flight symptoms" = panic attack.
Delirium	Specific causes include hypoglycemia, hypotension, hyperkalemia, hyponatremia, hypoxemia, high-dose corticosteroids.
Mania	Occurs in late HIV disease, probably a complication of organic brain disease. Symptoms include persistently elevated and expansive mood, less need for sleep, flight of ideas, grandiosity. Medications which can cause mania include ciprofloxacin.
Psychoses	Psychoses may be organic or functional. Medications which can cause psychoses include anabolic steroids, amphotericin B, ciprofloxacin, corticosteroids, dapsone, flucytosine, ganciclovir, INH, metronidazole, primaquine, sulfonamides, zidovudine.

* Adapted from L. Capaldini, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994.

NEUROPSYCHIATRIC SYNDROMES: PHARMACOLOGIC TREATMENT*

SYNDROME	AGENT	STARTING DOSE	THERAPEUTIC DOSE	COMMENTS
Depression	Tricyclic Antidepressants (sedating, anticholinergic effects)			
	Amitriptyline (Elavil)	10-25 mg po qhs [†]	150 mg po qhs	Morning somnolence, anticholinergic effects, may require 30 days for therapeutic effect
	Doxepin (Sinequan)	10-25 mg po qhs	150 mg po qhs	Morning somnolence
	Nortriptyline (Pamelor)	25-50 mg po qhs	75-100 mg po qhs	Least anticholinergic effects. Effective in painful neuropathy
	Desipramine (Norpramin)	25-50 mg po qhs	100-200 mg po qhs	Least sedating, effective in painful neuropathy
	Selective Serotonin Re-uptake Inhibitors (stimulant effect, sexual dysfunction, less risk of suicide with overdoses)			
	Fluoxetine (Prozac)	10-20 mg qAM	20-80 mg qd	If dose > 20 mg, give in AM and at noon. Most prone to cause stimulant symptoms (↑ anxiety). Full antidepressant effect may require 4 weeks.
	Sertraline (Zoloft)	25-50 mg qAM	50-200 mg qd	
	Paroxetine (Paxil)	10-20 mg qAM	20-50 mg qd	Full antidepressant effect may require 4 weeks.
	Chloropropiophenies (less sedating than tricyclics, less stimulant than SSRIs)			
	Bupropion (Wellbutrin)	100 mg bid	75-100 mg tid	Contraindicated in pts with unstable seizure disorders

[†] Abbreviations: qhs = taken at bedtime, qAM = taken upon arising, pm = taken as necessary (when symptoms require)

TABLE 7B (2)

SYNDROME	AGENT	STARTING DOSE	THERAPEUTIC DOSE	COMMENTS
Depression (continued)	Stimulants (especially good with despondency relating to medical illness)			
	Methylphenidate (Ritalin)	5 mg qAM	20-60 mg daily	Divide dosage tid
	Dextroamphetamine (Dexedrine)	5 mg qAM	5-40 mg daily	
	MAO inhibitors: Contraindicated			
AIDS Dementia	Zidovudine (Zovirax)	200 mg po tid		Higher dosage; 800-1200 mg may be necessary. See Table 7A, page 21
Anxiety	Anxiolytics			
	Clonazepam (Klonopin)	0.5 mg po q8h	0.5-2.0 mg q8h	Onset of action slow, long-acting (round the clock) (Not FDA-approved for this indication)
	Lorazepam (Ativan)	0.5-1.0 mg q8h prn	0.5-2.0 mg q8h prn	Rapid onset of action
	Alprazolam (Xanax)	0.25-0.5 q8h prn	0.5-1.0 mg q8h prn	Rapid onset of action
	Buspirone (BuSpar)	5 mg po tid	10-15 mg po tid	Non-sedating, non-addictive. Suitable for chronic anxiety
Delirium	Haloperidol (Haldol) + Lorazepam (Ativan)	2-5 mg IM (not IV q1-8h 2 mg IV		Correct specific cause if present
Mania	(Discontinue potential causative drugs)			
	Lithium	300 mg po tid	600 mg po tid	
	Carbamazepine (Tegretol)	200 mg po bid	400 mg po tid	Drug-drug interactions common, Table 19. Not FDA-approved for this indication.
	Valproic acid (Depakene)	250 mg po bid	250 mg tid	Drug-drug interactions common, Table 19. Not FDA-approved for this indication.
Psychoses	Low potency			
	Chlorpromazine (Thorazine, Mellaril)	25-50 mg q8-12h po	50-800 mg qd	Very sedating, anticholinergic side-effects. Low risk extrapyramidal symptoms
	Mid potency			
	Perphenazine (Trilafon)	4 mg po q8h	8-16 mg qd (in divided doses)	Medium risk for sedation, anticholinergic side-effects
	High potency			
	Haloperidol (Haldol)	0.5-2.0 mg po bid or tid	2-100 mg po qd (in divided doses)	Low risk for sedation, anticholinergic side-effects. High risk extrapyramidal symptoms. Case reports of neuroleptic malignant syndrome

TABLE 7C
PSYCHIATRIC AND NEUROLOGIC SIDE EFFECTS ASSOCIATED WITH ANTIRETROVIRAL DRUGS AND
DRUGS USED TO TREAT HIV-ASSOCIATED OPPORTUNISTIC INFECTIONS OR MALIGNANCIES

DRUG	SIDE EFFECTS	FREQUENCY/ SEVERITY
Acyclovir	Long-term administration (2 years): confusion, dizziness, hallucinations, paresthesias (~1%), somnolence, visual abnormalities	~1% +
Atovaquone	Headache, insomnia, dizziness (less than with TMP/SMX or pentamidine)	~10% ±
Azithromycin	Dizziness, headache (< 1%), vertigo, somnolence, hypoacusis [on high dose or prolonged regimens (0.5 gm, 30-90 days, 14%)]	Rare ±
Bleomycin	None causally associated	
Ciprofloxacin	Dizziness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor (↑ caffeine levels may exaggerate these side-effects, see Table 19, page 107), ataxia, convulsions, lethargy, drowsiness, weakness, paresthesias, depersonalization, depression	0.4% +
Clindamycin	? Neuro blockade in anesthesia (prolongation of apnea)	Rare ±
Clarithromycin	Headache (mild) 2%, hypoacusis (on high dose)	2% ±
Clofazimine	Dizziness, drowsiness, fatigue, headache, giddiness, taste disorder	< 1% ±
Didanosine (ddI)	Peripheral neuropathy 5-12% (major toxicity), headache 5%, seizure 3%, confusion 2%, insomnia 2%, anxiety 1%, nervousness 1%, dizziness 1%, abnormal thinking 1%, depression < 1%, taste perversion < 1%	5% ++
Doxorubicin	None causally associated	
Epoetin alfa	Headache, dizziness (occurred in equal frequency in placebo patients), seizures (10 cases reported, appear associated with underlying pathology)	15-20% ±
Ethambutol	Decreased visual acuity (optic neuritis, reversible); headache, dizziness, mental confusion, possible hallucinations	? ++
Etoposide (VP16)	Transient cortical blindness	Rare
Filgrastim (G-CSF)	None causally associated	
Fluconazole	Headache 1.9%	~2% ±
Flucytosine	Ataxia, hearing loss, headache, paresthesias, Parkinsonism, vertigo, confusion, hallucinations, psychosis	< 1% ±
Foscarnet	Seizures (10%, some related to underlying disease); > 5% headache, paresthesias, dizziness, neuropathy	5-10% ++
Ganciclovir	Abnormal thoughts, ataxia, coma, confusion, dizziness, headache, nervousness, paresthesias, psychosis, somnolence, tremor	5% +
Isoniazid	Peripheral neuropathy (↓ with pyridoxine, B6): convulsions, encephalopathy, optic neuritis, memory impairment, toxic psychosis	? +
Itraconazole	Headache 4%, dizziness 2%	~3% ±
Lamivudine (3TC)	Insomnia, headache	? ±
Marinol	Confusion, anxiety, hallucinations, depression	? ±
Ofloxacin	Dizziness, insomnia, hallucinations, paresthesias	1% +
Pentamidine	Confusion (hallucinations 1.7%, dizziness 0.5%)	~2% +
Primaquine	1 case report psychosis	? ±
Pyrimethamine	Insomnia, light-headedness, depression, seizures	Rare ±

TABLE 7C (2)

DRUG	SIDE EFFECTS	FREQUENCY/ SEVERITY
Rifabutin	Headache 3%, insomnia 1%	3% ±
Rifampin	Headache, drowsiness, ataxia, dizziness, mental confusion, behavioral changes	? ±
Sargramostim (GM-CSF)	None causally associated	
Stavudine (d4T)	Peripheral neuropathy, sleep disorders, mania	21% +
TMP/SMX	Aseptic meningitis, convulsions, ataxia, vertigo, tinnitus, headache, hallucinations, apathy, depression, nervousness	< 1% +
Trimetrexate	None causally associated	
Vinblastine	Paresthesias, peripheral neuritis, depression, convulsions	Uncom. +
Vincristine	Neuritic pain, sensory loss, paresthesias, ataxia, paralysis	Common ++
Zalcitabine (ddC)	Peripheral neuropathy (most frequent toxicity)	17-31% ++
Zidovudine (ZDV)	Headache, dizziness (at 500 mg/day, frequency equal to placebo patients). At higher doses: headache, dizziness, insomnia, paresthesias, somnolence	~ 5% +

TABLE 8
TREATMENT OF SPECIFIC INFECTIONS/MICROORGANISMS IN HIV+/AIDS PATIENTS

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial infections Bacillary angiomatosis (peliosis hepatis) [Bartonella (Rochalimaea) henselae, quintana] [Proposed taxonomic change: <i>Int J Sys Bact</i> 43:777, 1993]	Treatment	Erythromycin 500 mg po or IV qid weeks-months (see Comments) OR Doxycycline 100 mg po bid (see Comments)	Rifampin 600 mg po qd x 7-10 days	Clinical response in 3-4 days but requires up to 2 months to normalize lab parameters. Experience is more extensive with erythromycin than with doxycycline (<i>NEJM</i> 330:1509, 1994). Azithromycin (1.0 gm qd) reported effective in 1 case (<i>Clin Inf Dis</i> 17:264, 1993).
	Suppression	Erythromycin 250-500 mg qid (see Comments)		Life-long suppression may be necessary.
Campylobacteriosis (Campylobacter jejuni)		Ciprofloxacin 500 mg po bid x 7-10 d	Erythromycin 250 mg po qid x 7-10 days	CIP not approved for use in children or pregnant women. In children, an alternative is erythromycin. (Norfloxacin, ofloxacin reported effective but not FDA-approved for GI infections.)
Chlamydia trachomatis	Non-gonococcal or post-gonococcal urethritis, cervicitis	Doxycycline 100 mg bid po x 7 days or Azithromycin 1.0 gm po (single dose)	Erythromycin 500 mg qid po x 7 days or Ofloxacin 300 mg bid po x 7 days	Etiologies: Chlamydia 50%; other, ureaplasma, trichomonas, H. simplex virus (10-15%); remainder unknown. 6-10% of ureaplasma are resistant to tetracycline. If doxy fails, rx with erythromycin for 3 weeks.
Clostridium difficile		Metronidazole 250 mg qid (or 500 mg tid) po x 7-10 days	Vancomycin 125 mg qid po x 7-10 days	Also effective: bacitracin (po), see drug-associated diarrhea, page 34
Donovanosis (Calymmatobacterium granulomatis)	Granuloma inguinale	Doxycycline 100 mg bid po until all lesions healed (usually 1 week, but may require 4 weeks)	Trimethoprim-sulfamethoxazole 1 double-strength tablet (160 mg TMP) bid po	Rare in U.S. Response to rx should be seen in 7 days; if none, dx questionable. Treatment failures and recurrences seen with doxycycline.
Haemophilus ducreyi	Chancroid	Ceftriaxone 250 mg IM (single dose) or erythromycin 500 mg qid po x 7 days or ciprofloxacin 500 mg bid po x 3 days		Ciprofloxacin 500 mg po (single dose) has been effective in several clinical trials.
Klebsiella/Enterobacter	Stomatitis	P Ceph 3 or AP Pen or IMP or aztreonam or CIP. Use IV regimen		After starting empirical rx, when in vitro susceptibility results available select agent with narrowest spectrum of activity.
Listeriosis	Bacteremia, meningitis, focal infections	Ampicillin 200 mg/kg/d IV divided into q4h dosage	Trimethoprim/sulfamethoxazole 20 mg/kg/d TMP (component) IV divided into q6h dosage	Some evidence suggests synergy with ampicillin + an aminoglycoside (gentamicin). Duration of rx 2-4 weeks. (Cephalosporins not active vs L. monocytogenes.)
Lymphogranuloma venereum		Doxycycline 100 mg bid po x 21 days	Erythromycin 500 mg qid po x 21 days or sulfisoxazole 500 mg qid po x 21 days	Dx based on serology, biopsy contraindicated. Rectal LGV may require retreatment.

Abbreviations: po = orally, bid = 2x/day, tid = 3x/day, qid = 4x/day, qd = every day, qod = every other day or 3x/week, hs = at bedtime, P Ceph 3 = parenteral 3rd generation cephalosporin, AP Pen = antipseudomonal penicillin, IMP = imipenem cilastatin, CIP = ciprofloxacin, TMP = trimethoprim

TABLE 8 (2)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial Infections (continued)				
Mycobacterium tuberculosis	Preventive treatment, infection without disease (positive tuberculin test)* or HIV+ pt with energy and high risk for tuberculosis (<i>Ann Int Med</i> 119:185, 1993) Organisms likely to be INH-susceptible	Isoniazid (INH) 5 mg/kg/day (maximum 300 mg/day) po in adults + pyridoxine (B6) 25 mg po for 12 months. (If pt on ddC, 50 mg pyridoxine may be preferable). Higher dosage in infants and children, see page 90	Data on efficacy of alternative regimens is lacking. Regimens include ethambutol (15 mg/kg (maximum 1.0 gm) po qd] + rifampin 600 mg po qd 9-12 months or pyrazinamide [20 mg/kg (maximum dose 2.0 gm/d) po qd] + rifampin po qd x 2 months	Duration of rx not yet well defined; some recommend longer than 12 months (<i>MMWR</i> 38:247, 1989) while recent data suggest that 6 months may be adequate. RIF + PZA (2 months) vs INH + B6 (12 months) (ACTG 177) trial in progress. Some authorities prefer INH 900 mg po 2x/week as directly observed therapy (DOT). INH prophylaxis reported to ↓ progression of HIV (<i>Lancet</i> 342:268, 1993).
	INH-resistant, RIF-sensitive organisms likely	Rx indicated. See <i>Alternative and Comment</i>	Data on efficacy of alternative regimens currently lacking. Regimens include ETB + RIF daily for 6 mos., PZA + RIF daily for 2 mos., INH + RIF daily until susceptibility test results known, then if INH-CR, dc INH and continue RIF for 9 months, otherwise INH + RIF for 9 months (this latter is <i>Am Acad Pediatrics</i> ' 1994 recommendation). INH + RIF + ETB until sensitivities from index case (if known), then dc INH if totally resistant. Rx for 12 months.	
	INH and RIF-resistant organisms likely		Efficacy of alternative regimens is unknown: PZA (25-30 mg/kg/day po) + ETB (15-25 mg/kg/day po) (at 25 mg/kg ETB, monitoring for retrobulbar neuritis required), 12 months; PZA (20 mg/kg/d) + ETB (25 mg/kg/d) + ciprofloxacin (750 mg po bid) or ofloxacin (400 mg po bid) x 6-12 months (<i>Ann Int Med</i> 120:932, 1994).	
	Treatment, active tuberculosis Drug susceptible Isolation essential! (See Table 7A, page 37) Older observations on infectivity of susceptible and resistant M. tbc before and after rx (<i>Am Rev Resp Dis</i> 85:511, 1962) may not be applicable to MDR M. tbc or to the HIV+ individual. Extended isolation may be appropriate.	If out of hospital: directly observed rx 2-3x weekly is preferred unless compliance is quite certain. Isoniazid (INH) 5 mg/kg/d (maximum 300 mg) po as a single daily dose + Rifampin (RIF) 10 mg/kg/d (maximum 600 mg) po or IV as a single daily dose + Pyrazinamide (PZA) 15-25 mg/kg/d (usually 2.0 gm) po as a single daily dose with or without Ethambutol (ETB) 15 mg/kg/d (usually 1.5 gm) po as a single dose + Pyridoxine (B6) 25 mg po qd (if pt on ddC, 50 mg po qd). (can't on next page)	Intermittent regimen (twice weekly): Begin as standard regimen for 2 weeks to 2 months, then INH 900 mg po + RIF 600 mg po twice weekly (<i>Am Rev Resp Dis</i> 134:355, 1986). In non-HIV+ pts, regimen of DOT 3x weekly has been used from onset.	Clinical and microbiologic response the same as in HIV- pt. If INH or RIF not used, rx at least 18 months and 12 months after cultures negative. In absence of poor compliance or drug resistance, sputum cultures should become negative after 5-6 months rx. On standard regimen (INH+RIF+PZA) relapse rate ~5%. Maintenance rx not required (<i>NEJM</i> 324:289, 1991). Pts with AIDS enteropathy may have malabsorption of anti-TB drugs, in pt with diarrhea monitoring of blood levels may be of value (<i>NEJM</i> 327:1817, 1992). 60-70% of HIV+ pts with TB have extrapulmonary involvement. HIV pts with active pulmonary TB may be highly infectious for other HIV+ pts and staff (50% in one report) with active disease developing rapidly (within 4 weeks) (<i>NEJM</i> 326:231, 1992). In the past, pts under rx for TB have been housed together, individuals with active TB were not susceptible to superinfection. HIV+ pts with drug-susceptible M. tbc on treatment are susceptible to infection with drug-resistant M. tbc if exposed (<i>NEJM</i> 328:1137, 1993). In HIV- pts corticosteroids often used with pericardial effusion, meningitis or severe (Continued on next page)

* Tuberculin test: The standard is the Mantoux test, 5 TU PPD in 0.1 ml diluent stabilized with Tween 80. Read at 48-72 hrs, measuring the maximum diameter of induration (not erythema). A reaction of ≥ 5 mm is defined as + in the HIV+ patient. Abbreviations: ddC = zalcitabine, SM = streptomycin, MDR M. tbc = multidrug resistant M. tuberculosis, INH-CR = complete INH resistance; DOT = directly observed therapy; INH = isoniazid; RIF = rifabutin; ETB = ethambutol; PZA = pyrazinamide

TABLE 8 (3)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial infections (continued)				
Mycobacterium tuberculosis (continued)	Treatment, active tuberculosis Drug susceptible (continued)	(continued from above) INH + RIF + PZA for 2 months then INH + RIF for 4 months=total 6 months or until 6 months after culture negative, 6 months if ETB used.	(As above)	drug reactions. In HIV+ pts, steroid-treated pts showed greater improvement in lymphadenopathy and cough but ↑ herpes zoster and possibly Kaposi's sarcoma (Quart J Med 85:855, 1992).
	Suppression	Usually not required for drug-susceptible M. tbc		NEJM 324:269, 1991. Recurrence rates ↑ in pts rx with thiacetazone regimens (Lancet 342:332, 1993)
	Multidrug resistant (MDR), i.e., resistant to INH, RIF, SM, ETB and/or PZA	Satisfactory regimens have not been defined, most agree that an injectable agent (amikacin, capreomycin or kanamycin) should be included. Regimens should include 2-3 drugs to which the isolates are susceptible. One regimen is: CIP (750 mg bid) + ETB (15 mg/kg/ d) + RIF (600 mg/d) + amikacin (7.5 mg/kg q12h IM) (Ann Int Med 120:945, 1994).	Another regimen is amikacin (7.5 mg/kg q12h IM) + CIP (750 mg bid po) + ETB (15 mg/kg/d po) + [PZA (15-25 mg/kg/d po)]. Consider rifabutin as alternative to RIF (~ 30% RIF-resistant strains are sensitive to rifabutin).	Isolation! (See Comments, above.) By September 1992 clusters of multidrug resistant (MDR) TB reported in 14 U.S. hospitals and 1 prison system (Ann Int Med 118:77, 1993) had been studied, most strains were resistant to INH & RIF but many to INH, RIF, SM, ETB and PZA, up to 7 drugs. Transmission to other pts, health care workers and family reported. Mortality rates in this type of disease were 70-90% with median 4-16 weeks from diagnosis to death (NEJM 326:703, 1992). Prompt identification and isolation is essential! Imipenem is active in vitro and being used in some regimens (not an FDA-approved indication). The investigational fluoroquinolone, sparfloxacin is very active in vitro vs M. tuberculosis.
Mycobacterium avium-intracellulare complex (MAI or MAC)	Primary prophylaxis (It is essential to exclude active tuberculosis before rifabutin monotherapy--will promote development of rifampin-resistant strains)	Rifabutin (300 mg po qd)	Trials in progress with: (1) clarithromycin 500 mg po bid vs placebo, (2) [azithromycin (1200 mg po weekly) + fluconazole] vs [azithromycin + rifabutin + fluconazole] vs [rifabutin + fluconazole], (3) azithromycin 500 mg 3x weekly.	MAC frequently isolated from sputum (12%) or stools (10%). Risk of bacteremia is ~ 60% within 1 yr but culture of sputum or stool has limited usefulness as screening test (J Inf Dis 169:289, 1994). Rifabutin approved as prophylaxis in HIV+ with CD4 < 200/mm ³ (NEJM 329:828, 1993). Efficacy in 2 studies: MAC bacteremia in 8% on rifabutin vs 17% on placebo (ACTG 023) and 9% on rifabutin vs 18% on placebo (ACTG 027) (over 1100 pts) (NEJM 329:828, 1993). Adverse reactions requiring discontinuation of rifabutin in 16% (see Table 9, page 76), placebo 8%. The Public Health Service Task Force recommends prophylaxis when CD4 < 100/mm ³ (NEJM 329:898, 1993), other authorities at CD4 < 50 while others do not recommend. Rifabutin ↑ metabolism of ZDV with 32% ↓ in AUC.

Abbreviation: AUC = area under the curve (blood concentration vs time)

TABLE 8 (4)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial infections (continued)				
Mycobacterium avium-intracellulare complex (MAI or MAC) (cont')	Treatment (positive cultures of blood, bone marrow, other usually sterile body fluids, organ tissue (e.g., liver))	Optimal regimens still not defined. Clarithromycin 500 mg bid po (or azithromycin 500 mg qd po) + ethambutol 15-25 mg/kg qd po. Some authorities add rifabutin 300 mg qd po (see Comments) or clofazime 100-200 mg qd po or ciprofloxacin 750 mg bid or qd po.		MAI seldom seen with CD4 > 100/mm ³ (NEJM 324:1332, 1991). Pts who develop MAC on rifabutin prophylaxis should receive same regimen. Value of in vitro sensitivity testing is unknown. Clarithro ↓ absorption of ZDV (20% ↓), separate dosing by several hours. Ethambutol dosage of 25 mg/kg qd should not exceed 1 month. On treatment with rifabutin as recommended (600 mg qd, in combination with clarithro + ethambutol), about 1% pts developed uveitis (recommended dose now ↓ to 300 mg qd) (NEJM 330:438, 1994).
	Suppression (secondary prophylaxis)	If clinical and microbiologic improvement observed, continue tx indefinitely		Recurrences common in bacillemic patients. Lifelong suppression seems rational but definitive studies on efficacy and safety not yet available.
Mycobacterium kansasii	Treatment	Rif (600 mg po qd) + ETB (15 mg/kg/d po) + INH (5 mg/kg/d po) for 15-18 months (Ann Int Med 120:945, 1994)	In pts who do not respond, add sulfamethoxazole (or TMP/SMX) (Rev Inf Dis 13:789, 1991)	If organism resistant to (≥ 1 µg/ml) INH, discontinue INH (70-85% isolates are resistant). Almost all isolates resistant to PZA. Rx a minimum of 15 months after culture negative. M. kansasii sensitive in vitro to clarithro (MIC ≤ 2.0 µg/ml), erythromycin, amikacin.
Mycobacterium chelonae	Treatment	Clarithromycin (500 mg po bid x 6 months effective in HIV- pts). M. chelonae sensitive in vitro to neomacrolides, resistant to fluoroquinolones.		
Mycobacterium fortuitum	Treatment	Optimal regimen not defined. Amikacin + cefoxitin + probenecid 2-6 weeks, then po TMP/SMX, doxycycline or erythromycin 2-6 months (J Inf Dis 152:50, 1985). Trials with neomacrolides indicated. Surgical excision of infected areas.		Resistant to all standard anti-TBc drugs. Sensitive in vitro to cefoxitin, imipenem, amikacin, TMP/SMX, CIP, oflox, clarithromycin
Mycobacterium haemophilum	Treatment	Regimen(s) not defined		Clinical: Ulcerating skin lesions, synovitis, osteomyelitis. Lab: Requires supplemented media to isolate. Sensitive in vitro to: CIP, cycloserine, rifabutin. Over ½ resistant to: INH, RIF, ETB, PZA (Ann Int Med 120:118, 1994).
Mycobacterium genavense	Treatment	Regimen(s) not defined		Clinical: CD4 < 50. Symptoms of fever, weight loss, diarrhea. Lab: growth in BACTEC vials slow (mean 42 days). Subcultures grow only on Middlebrook 7H11 agar containing 2 µg/ml mycobactin J—growth still insufficient for in vitro sensitivity testing (Lancet 340:76, 1992; Ann Int Med 117:586, 1992).
Mycobacterium gordonae	Treatment	Regimen(s) not defined		In vitro: sensitive to ethambutol, rifampin, amikacin, ciprofloxacin, clarithromycin. Resistant to INH (Clin Inf Dis 14:1229, 1992).
Mycobacterium marinum	Treatment	RIF + ETB or minocycline or TMP/SMX for 6 weeks (Arch Int Med 147:817, 1986)		Sensitive in vitro to clarithromycin, reported effective in 2 pts (1 HIV+ who failed on other regimens) (Clin Inf Dis 18:664, 1994).
Mycobacterium simiae	Treatment	Regimen(s) not defined		In vitro: sensitive to sulfamethoxazole, ciprofloxacin. Resistant to INH, rifampin, ethambutol, kanamycin and clarithromycin (Clin Inf Dis 17:508, 1993)

Abbreviations: neomacrolides = azithromycin, clarithromycin, roxithromycin; TMP/SMX = trimethoprim/sulfamethoxazole

TABLE 8 (5)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial Infections (continued)				
Mycobacterium xenopi	Treatment	Regimen(s) not defined		In vitro: sensitive to clarithromycin (<i>Antimic Ag Chemo</i> 36:2841, 1992)
Neisseria gonorrhoeae (gonococcus)	Gonorrhea; urethritis, conjunctivitis, proctitis; mucopurulent cervicitis; epididymoorchitis (sexually acquired)	Ceftriaxone 125 mg IM (single dose) or Cefixime 400 mg po x 1 dose or Ciprofloxacin 500 mg po x 1 dose or Ofloxacin 400 mg po x 1 dose + Doxycycline 100 mg bid po x 7 days	Norfloxacin 800 mg po x 1 dose or Spectinomycin 2.0 gm IM x 1 dose	50% of patients have concomitant C. trachomatis, treatment regimens should include rx for C. trachomatis (above). Ciprofloxacin or ofloxacin should not be used in pregnant women or in children. Spectinomycin not effective in gonococcal pharyngitis; for pharyngeal infection use ceftriaxone or ciprofloxacin.
Pelvic inflammatory disease (PID), salpingitis, tuboovarian abscess. Etiology polymicrobial: gonococcus, C. trachomatis, bacteroides, enterobacteriaceae, streptococci, mycoplasma	Outpatient (limit to patients with temp < 38°C, WBC < 11,000/mm ³ , minimal evidence of peritonitis, active bowel sounds & able to tolerate oral nourishment	Ceftriaxone 250 mg IM single dose plus doxycycline 100 mg bid po x 14 days or Cefoxitin* 2.0 gm IM single dose plus probenecid 1.0 gm concurrently plus doxycycline or Ofloxacin 400 mg bid po x 14 days + clindamycin 450 mg qid po or metronidazole 500 mg bid po x 14 days	Amoxicillin/clavulanate 500 mg tid po x 14 days plus doxycycline	Indications to hospitalize: compliance as an outpatient unlikely, pregnant, peritonitis, suspected pelvic abscess, temp > 38°C, need for laparoscopy to clarify diagnosis, failure to respond as outpatient in 72 hours, diagnosis uncertain. If patient should be hospitalized but cannot be, add metronidazole 0.5 gm bid po. 15/16 pts with tuboovarian abscess successfully rx with antibiotics + CT-directed needle drainage (<i>Radio</i> 182:399, 1992).
	Hospitalized	Cefoxitin* 2.0 gm q6h IV plus doxycycline 0.1 gm IV or po q12h. Rx at least 4 days and afebrile for 48 hrs. After IV rx, doxy 0.1 gm bid po or clinda 0.45 gm qid po to complete 14 days	Clindamycin 900 mg q8h IV plus gentamicin (2.0 mg/kg initial dose then 1.5 mg/kg q8h IV) (can be given in same IV). Rx as with cefoxitin. Follow with oral agent (doxycycline) to complete 14 days.	
Prostatitis, acute; Etiologies: N. gonorrhoeae, C. trachomatis	Age usually ≤ 35 years	Treat as gonorrhea: ceftriaxone followed by doxycycline or azithromycin (see above)		Each of the fluoroquinolones is active vs N. gonorrhoeae. Ofloxacin is more active vs C. trachomatis than ciprofloxacin, which is marginal. Norfloxacin is not active. If it cannot be determined whether N. gonorrhoeae, C. trachomatis or enterobacteriaceae is involved, ofloxacin provides the broadest coverage. Overall cure rates vs enterobacteriaceae ~ 80%. Although azithro has some in vitro activity vs E. coli, it is not appropriate for monotherapy. In AIDS patients, the prostate may be a focus of Cryptococcus neoformans despite fluconazole suppression (<i>Ann Int Med</i> 115:285, 1991).

* Alternative agents: Cefotetan 2.0 gm IV q12h; cefmetazole 2.0 gm IV q6h

TABLE 6 (6)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial infections (continued)				
Prostatitis, acute (cont) Enterobacteriaceae	Age usually > 35 years	Norfloxacin 400 mg bid po or Ciprofloxacin 500 mg bid po x 4-6 weeks or Ofloxacin 300 mg bid po x 6 weeks	TMP/SMX (1 ds bid po). If chronic, rx for 3 months	
Rhodococcus sp. (Corynebacterium equi)	Pulmonary	Vancomycin 1.0 gm IV q12h for at least 2 weeks	Erythromycin (0.5 gm IV q6h) or imipenem (0.5 gm IV q6h) + rifampin 600 mg po qd for at least 2 weeks or ciprofloxacin 750 mg bid po	3/4 pts have positive blood cultures (Rev Inf Dis 13:91, 1991). Prolonged oral suppressive therapy (macrolide + rifampin) may be useful since relapses are frequent.
Salmonella sp.	Bacteremia, recurrent	Ciprofloxacin (CIP) 750 mg po bid x 14 days. If relapse occurs, CIP 500 mg po bid indefinitely	If isolates sensitive, ampicillin or trimethoprim/sulfamethoxazole	Norfloxacin, ofloxacin, lomefloxacin, and ceftriaxone are effective in vitro but not approved by FDA for rx of GI infections. Ciprofloxacin-resistant strains of salmonella have been reported.
	"Sepsis"/Bacteremia	Multiple regimens recommended; the most commonly used is a beta-lactam plus an aminoglycosidic antibiotic. Monotherapy or double beta-lactam regimens also have been effective. One regimen widely used is aminoglycoside + [antipseudomonal penicillin or antipseudomonal 3rd generation cephalosporin] with or without vancomycin added initially. Imipenem has been effective as monotherapy. If pt colonized with candida, add amphotericin B.		
Shigellosis	Treatment Acute	Ciprofloxacin (500 mg po bid) x 5-7 days		Norfloxacin, ofloxacin and lomefloxacin are effective in vitro but not approved by FDA for rx of GI infections.
	Recurrent	Ciprofloxacin 500 mg po bid (perhaps 750 mg po qd) indefinitely		
Staphylococcus aureus	Treatment: Folliculitis Ecthyma	Dicloxacillin 500 mg po qid for 7-14 days. If refractory/ recurrent, add rifampin 600 mg po qd	Erythromycin 500 mg po qid for 7-14 days or Mupirocin (Bactroban), apply to affected area tid for 5 days (if infection not disseminated)	
	Suppression: Recurrent infections (most likely pt is a nasal carrier)	Mupirocin (Bactroban), apply to nasal vestibule tid x 10 days	Dicloxacillin 500 mg qid po + rifampin 600 mg po qd x 10 days	Culture nasal vestibule to determine if nasal carrier. Effective vs both MSSA and MRSA.
Streptococcus pneumoniae	Suppression: Recurrent pneumococcal infections	Penicillin VK 250 mg po bid indefinitely	In penicillin-allergic patient: erythromycin, neomacrolides, clindamycin	All HIV+ pts should receive pneumococcal vaccine. See Tables 2, 13. Administer vaccine early, as antibody responses ↓ as CD4 counts decrease.

Abbreviations: MSSA = methicillin-sensitive Staph. aureus; MRSA = methicillin-resistant Staph. aureus; Neomacrolides = azithromycin, clarithromycin, roxithromycin

TABLE 8 (7)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Bacterial infections (continued)				
<i>Streptococcus pneumoniae (continued)</i>				
Pneumonia—not life-threatening	Treatment	Ceftriaxone 1.0 gm q12h IV or cefotaxime 1.0 gm q8h IV	Penicillin G 20 million units/day IV or erythromycin 500 mg qid po	Community-acquired drug-resistant <i>S. pneumoniae</i> (DRSP) is emerging as a widespread problem in the U.S. (MMWR 43:23, 1994) and is a major problem in Spain, France and Hungary. Penicillin resistance (most common in U.S.) is classified into 2 types: relative-level resistance (RLR) (MIC for penicillin G > 0.1 μ g/ml but $\leq$ 1.0 μ g/ml) and high-level resistance (HLR) (MIC for penicillin G $\geq$ 2.0 μ g/ml). DRSP seen in 30–60% isolates from children in day care centers in several states. About 1/2 DRSP show RLR. These are clinically important in meningitis, other sites can be treated with high doses. 1/2 DRSP have HLR, of these 1/4–1/2 are resistant to cefotaxime (AAC 37:1630, 1993). Of all DRSP isolates, 1/4–1/2 are resistant to erythromycin, TMP/SMX and chloramphenicol. All have been sensitive to vancomycin and rifampin.
Pneumonia—life-threatening	Treatment	Vancomycin 1.0 gm q12h IV		
Meningitis	Treatment	Vancomycin 1.0 gm q12h IV + rifampin 600 mg po qd + ampicillin 200 mg/kg qd IV		
Syphilis (<i>Treponema pallidum</i>)		Recommendations vary; most use standard regimen: <i>Early: primary, secondary, latent</i> < 1 yr—Benzathine penicillin G 2.4 million units IM. <i>More than 1 yr's duration (latent of indeterminate duration, cardiovascular, or late benign)—Benzathine penicillin G 2.4 million units IM q weekly x 3 (7.2 mu total)</i>	Penicillin G 10–12 mu IV qd x 14–21 days or Supplement "standard" with amoxicillin (2.0 gm po tid) + probenecid (0.5 gm po tid) x 10 d or Ceftriaxone 250 mg IM qd x 10 d	Clinical presentations, serology and response to rx may be atypical. Higher doses and longer periods of rx may be required. Repeat VDRL (RPR) at 3, 6, 12, 24 months. Retreat if (1) clinical signs persist or recur, (2) a sustained 4-fold $\uparrow$ in VDRL titer occurs, (3) an initial high titer fails to $\downarrow$ to < 1:8 at 1 yr. Reinfection with <i>T. pallidum</i> not uncommon. Erythromycin should not be used as an alternative agent. Desensitization to penicillin may be required. Doxycycline has been used in preference to erythro if unable to desensitize. Re-treat if needed (<i>Am J Med</i> 93:477, 1992).
	Neurosyphilis	Penicillin G (aqueous crystalline pen G 12–24 million units IV/day x 10 days followed by benzathine pen G 2.4 million units IM weekly x 3 doses	Chloramphenicol (0.5 gm po qid x 10 days) or Ceftriaxone (1.0 gm IM or IV qd x 14 days)	
Bacterial vaginosis		Metronidazole 0.5 gm bid po x 7 days or metronidazole 2.0 gm po as single dose or metronidazole vaginal gel (0.75%) 1 applicator (5 gm) intravaginally bid x 5 days	Clindamycin 0.3 gm bid po x 7 days or clindamycin cream (2%) 1 applicator (5 gm) intravaginally hs x 7 days	Metronidazole; avoid in 1st trimester of pregnancy. Based on recent analysis, metronidazole 2.0 gm po single dose may be as effective as 5–7 day course (JAMA 268:92, 1992). NOTE: Product labeling gives dosage as q6h but CDC 1993 STD Guidelines recommend bid dosage.

Abbreviations: VDRL (RPR) = non-treponemal serologic tests for syphilis (in contrast to FTA/ABS test)

TABLE 8 (8)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Fungal infections				
Aspergillosis	Sinusitis and/or pneumonia	Amphotericin B 0.5–1.0 mg/kg qd IV until objective evidence of response, then 0.8 mg/kg qod IV. Total dose not defined.	Itraconazole 200 mg bid po has been used but response is poor. Duration of rx not yet defined.	Lifelong suppressive therapy likely needed. No proven regimen yet defined. Suggest: Amphotericin B 1.0 mg/kg IV 1–3 times/week. With itraconazole, absorption shows marked variation. Serum levels of $\geq 5 \mu\text{g/ml}$ required for predictable efficacy.
Blastomycosis		Amphotericin B 0.5–1.0 mg/kg IV until evidence of response, then itraconazole 200 mg/d po with breakfast		In HIV+ pt, itraconazole is drug of choice (<i>Am J Med</i> 93:489, 1992). Experience in HIV+ pts is limited, hence more traditional regimen is recommended.
Candidiasis	Bloodstream, associated with venous catheters (no metastatic lesions)	Amphotericin B 0.4 mg/kg/d. Total dose 7 mg/kg.	Fluconazole 400 mg po 1st day, then 200 mg po qd x 4 weeks	Treat all positive blood cultures, do not assume candidemia is a benign condition! In one series 9/32 (28%) with candidemia developed endophthalmitis (<i>Arch Int Med</i> 149:2226, 1989). A total dose of amphotericin B of 3 mg/kg has been recommended but failures (endophthalmitis and hepatic abscesses) reported, hence the higher dosage is recommended.
	Metastatic lesions; endophthalmitis and/or hepatosplenic	Amphotericin B 0.6 mg/kg/d IV for 7 days followed by 0.8 mg/kg qod IV until definite evidence of resolution. Most pts should receive 0.5–1.0 gm total dose (<i>Clin Inf Dis</i> 14:5106, 1992)	Fluconazole 400 mg po on 1st day then 200 mg po qd x 6–8 weeks (see Comments)	Ophthalmologic consultation is critical for determining if vitrectomy indicated. Role of fluconazole in endophthalmitis is not defined (its use is not clearly stated as an FDA-approved indication). In hepatosplenic candidiasis, 20/22 pts (most of whom failed to respond or had serious toxicity with amphotericin B) responded to fluconazole 200–400 mg po qd x 6–12 months (<i>Am J Med</i> 91:137, 1991; <i>ibid.</i> , p. 142).
	Oral and/or esophageal	Fluconazole 200 mg po 1st day then 100 mg qd until improvement (3–4 days) then continue suppressive rx, 150 mg po q week (<i>Med J Aust</i> 158:312, 1993). Some authorities would not treat asymptomatic patients or would use topical drugs		If no response in 1 week, change to amphotericin B (0.3 mg/kg IV qd x 7 days). Fluconazole contraindicated vs <i>C. krusei</i> (primary resistance). Secondary resistance vs flucon reported with <i>Torulopsis glabrata</i> and uncommonly with <i>C. albicans</i> . Ketoconazole may be contraindicated vs <i>C. tropicalis</i> . Itra resistance not reported (<i>J Antimicrob Chem</i> 31:463, 1993). Fluconazole-resistant <i>C. albicans</i> may be susceptible to itra.
			Clotrimazole troches (10 mg) one 5x/day Nystatin solution or tablets 500,000–1,000,000 units "swish and swallow" 3–5 x/day x 14 days	
	Intestinal	Same as oral and/or esophageal		
	Urinary (bladder, not renal)	Remove indwelling catheter if possible (spontaneous clearing then likely). If catheter can't be removed or funguria persists: Fluconazole 200 mg 1st day, then 100 mg qd x 3–5 days (this is not an FDA-approved indication)	The hazard of candiduria as a focus for systemic infection is not well defined but appears to be low (<i>Clin Inf Dis</i> 17:1066, 1993); however, many clinicians will attempt to clear the urine. Amphotericin B (bladder irrigation): Irrigate/instill 200–300 ml of amphotericin B in 5–10 mg/L of sterile water, then cross-clamp the catheter for 60–90 minutes, then allow the bladder to drain and repeat the procedure. If infection is limited to the bladder, 2 days rx should suffice (<i>Clin Inf Dis</i> 16:145, 1993). The usually recommended dosage is 50 mg/1000 ml sterile water; this concentration may be toxic to uroepithelium and not required.	

TABLE 8 (9)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Fungal infections (continued)				
Candidiasis (continued)	Vaginal	Topical (vaginal): Miconazole nitrate 200 mg vaginal tabs (1 qd hs x 3 days) or 2% cream (5 gm) qd hs x 7 days Clotrimazole 100 mg vaginal tabs (2 qd hs x 3 days) or 1% cream (5 gm) qd hs x 7 days Butoconazole 2% cream (5 gm) qd hs x 3 days Terconazole 80 mg vaginal tab (1 qd hs x 3 days) or 0.4% cream (5 gm) qd hs x 7 days Tioconazole 300 mg vaginal ointment x 1 dose Oral: Fluconazole 150 mg po qd x 3 d (<i>Brit J Ob Gyn</i> 96:226, 1989) (Not an FDA-approved indication) Itraconazole 200 mg po qd x 3 d (<i>Antimicro Ag Chemo</i> 37:89, 1993) (Not an FDA-approved indication)		Cure aided by avoiding tight clothing, e.g., pantyhose. Cure rates between imidazoles are comparable (85-90%), more effective than nystatin. Many pts prefer oral rx. Oral drugs ↓ rectal candida and may ↓ relapses. In HIV+ pt, suppressive rx with fluconazole (50 mg po 3x/week and 200 mg po 1x/week) are under study.
Coccidioidomycosis	Primary prophylaxis	Under study, currently not recommended		Fluconazole 200 mg po qd indefinitely (2 years) is under study in a placebo-controlled trial.
Pulmonary and Extra-pulmonary (not meningitis)	Treatment	Amphotericin B 0.6 mg/kg/d IV x 7 days, then 0.8 mg/kg qod. Total dose 2.5 gm	Fluconazole 400-800 mg po qd for 8 weeks	Itraconazole 200 mg po q12h resulted in 72% response rate in 72 non-HIV+ pts (<i>J Am Acad Derm</i> 23:593, 1990) (Not an FDA-approved indication).
Meningitis	Treatment	IV amphotericin B as above plus 0.1-0.3 mg daily intrathecal (intraventricular via reservoir device)		There are reports of coccidioidal meningitis responding to both fluconazole and itraconazole, but these are too preliminary to alter recommendations (<i>Clin Inf Dis</i> 13:S100, 1992).
Coccidioidomycosis	Suppression	Amphotericin B 1.0 mg/kg once/week IV or Itraconazole 200 mg bid po (<i>Ann Int Med</i> 120:932, 1994)	Fluconazole 400 mg/day po or Ketoconazole 400 mg/day po indefinitely	As with many other infections, relapses are common in the HIV/AIDS patient. On the basis of retrospective analyses, amphotericin B is preferred by some authorities (<i>Clin Inf Dis</i> 14:5154, 1992).
Cryptococcosis	Primary prophylaxis	Authors do not currently recommend primary prophylaxis. In non-randomized study, pts with CD4 < 68 rx with fluconazole 100 mg po qd, 1/329 developed cryptococcosis vs 16/337 historical controls (<i>AIDS</i> 6:191, 1992). A randomized trial comparing fluconazole 200 mg po qd with clotrimazole 50 mg po qd (ACTG 981) demonstrated a significant ↓ in invasive mycoses with fluconazole especially in cryptococcosis but did not increase survival.		

TABLE 8 (10)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Fungal infections (continued)				
Cryptococemia (positive blood culture or positive serum cryptococcal antigen test) and/or Meningitis	Treatment	Amphotericin B (initial rx) with fluconazole completion rx. Ampho B: 0.5–0.8 mg/kg/d IV until afebrile, headache, nausea and vomiting gone. Then dc ampho B, start flucon 400 mg po qd to complete 8–10 week course. Then maintain on flucon 200 mg po qd indefinitely. If ampho B only, total dose 2.5 gm.	Fluconazole 400 mg po qd x8–10 weeks, then suppressive rx. Many authorities would use ampho B + flucytosine 37.5 mg/kg q6h po until patient afebrile and cultures negative (~6 weeks).	Most authorities would now rx all patients with ampho B initially although if pt has mild disease (normal mental status, CSF > 20 cells/mm ³ , CSF crypto antigen < 1:1024) some would use fluconazole alone. Serial monitoring of crypto antigen titers has limited role (no correlation between serum titer changes and outcome, stable or ↑ CSF titers correlate with failure (<i>Clin Inf Dis</i> 14:789, 1994). Flucytosine levels must be measured; adjust dose to give serum levels: peak 70–80 mg/L, trough 30–40 mg/L. With ampho B, dose of flucyt usually needs to be ↓. Early studies with fluconazole + flucytosine are encouraging. CSF cultures negative at 10 weeks in 20% pts on fluconazole vs 55% on flucon + flucyt. With lower dose ZDV, flucyt hematotoxicity is less of a problem.
Cryptococcosis	Suppression	Fluconazole 200 mg/d po indefinitely (lifetime)		Itraconazole 200 mg qd po may be as effective as fluconazole.
Fusariosis		Amphotericin B (dosage as in coccidioidomycosis)		Clinical: Focal, sometimes blackened skin lesions, fungemia. Ampho B occasionally effective, but mortality ~ 75%.
Histoplasmosis	Primary prophylaxis	Not indicated		
Progressive, disseminated	Treatment	Amphotericin B 50 mg qd IV (or 1 mg/kg if < 50 kg) x 2 weeks, then 50 mg IV qod to total dose of 10–15 mg/kg, then begin suppressive therapy	Itraconazole: 300 mg po bid x 3 d, then 200 mg po bid for 12 weeks, then 200 mg po qd with breakfast for 12 months (ACTG 120). 51/61 (88%) pts responded (cleared fungemia) [32nd ICAAC (Abst. 1206):312, 1992]. Some now consider itra the drug of choice.	Most patients who receive at least 500 mg amphotericin B do well initially, failure rate ~ 10% (<i>Med</i> 69:367, 1990), but relapse rates are 35–80%. With suppressive amphotericin B rx, relapse rate is 10–20% (<i>Clin Inf Dis</i> 14:S60, 1992). Ketoconazole is not effective rx (failure rate 90%). Fluconazole failure rate ~ 30% (ACTG 174).
	Suppression	Itraconazole 200 mg po bid indefinitely	Amphotericin B 50 mg IV weekly or biweekly indefinitely (lifetime)	10–20% relapses with ampho B, 60% with ketoconazole. Itraconazole: 2/42 (5%) pts relapsed with median follow-up 2 yrs (ACTG 084) (<i>Ann Int Med</i> 118:610, 1993).
Penicillium marneffei	Treatment	Amphotericin B 0.5–1.0 mg/kg qd IV until response, then 0.8 mg/kg qod	Itraconazole 300 mg bid po x 3 days, then 200 mg bid po x 12 weeks, then 200 mg po qd	16 of 21 pts responded to ampho B, 6 of 7 to itra (<i>J AIDS</i> 6:466, 1993). Resistance to ampho B, sensitivity to itra reported (<i>Clin Inf Dis</i> 15:744, 1992). Prolonged suppressive rx probably required.
Sporotrichosis	Treatment	Amphotericin B 0.4–0.6 mg/kg qd IV x 2 weeks, then 0.8 mg/kg qod. Total dose 1.5 gm		It is not clear whether or not post-treatment suppressive rx is needed.
Trichosporon beigeli, Scedosporium inflatum		Miconazole 1200–2400 mg/d IV divided into 3 doses for 6 to 20 weeks	Ketoconazole	These fungi emerging as opportunistic pathogens are resistant to amphotericin B. Efficacy of miconazole and ketoconazole not proven.

TABLE 8 (11)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Parasitic infections				
Protozoan				
Blastocystis hominis	Intestinal	Metronidazole 750 mg po tid x 10 days	Iodoquinol 650 mg po tid x 20 days	Whether or not <i>B. hominis</i> has a causal role in diarrhea has not been established (<i>Rev Inf Dis</i> 10:930, 1988), hence rx is questionable (<i>Ann J Gastroenterol</i> 87:729, 1992).
Cryptosporidium sp.	Treatment	There is no standard treatment; paromomycin 500–750 mg po tid or qid for 10 days to several months or 1.0 gm po bid x 1 month has anecdotal support		No antimicrobial agent shown to be effective in controlled trials. Paromomycin: 16/23 responded, 6/9 relapsed. In recent report 7/7 responded, 2/7 relapsed on long-term rx (<i>Clin Inf Dis</i> 16:298, 1993) and 22/24 responded clinically with complete remission in 18 (on 1.0 gm po bid, lag time before response 10 days) (<i>Clin Inf Dis</i> 18:447, 1994). 1 of 4 pts with cryptosporidial cholangitis responded. Current trials include azithromycin (900–1800 mg qd x 2–4 weeks), paromomycin (ACTG 192), diclazuril, letrozuril (10–100 mg po qd x 3 weeks, ACTG 198), atovaquone (750 mg po qid). Symptomatic rx with Imodium, diphenoxylate, tincture of opium or octreotide. Octreotide (Sandostatin) 50 µg sc q8h x 48 hrs, if no response ↑ stepwise to 500 µg q8h. 42% pts responded with ↓ diarrhea (<i>Ann Int Med</i> 115:705, 1991).
	Suppression	Modify paromomycin as required		
Entamoeba histolytica	Asymptomatic "carrier"	Paromomycin 500 mg po tid x 7 days or Iodoquinol 650 mg po tid x 20 days	Diloxanide furoate 500 mg po tid x 10 days	Clearance rates of 75–96% reported. Treat infected partners. Retreatment often required.
	Symptomatic intestinal (dysenteric) and/or extraintestinal	Metronidazole 750 mg po tid x 10 d followed by Iodoquinol 650 mg po tid x 20 days	Metronidazole as in primary followed by Paromomycin 500 mg po tid x 7 days	Tinidazole ^{NLS} 2.0 gm po qd x3 days for mild intestinal disease, 600 mg po bid x5 days for severe intestinal, 800 mg po tid x5 days for extraintestinal.
Giardia lamblia		Metronidazole 250 mg po tid x 5 days	Quinacrine (Mepacrine in Europe) 100 mg po tid after meals x 5 days or tinidazole ^{NLS} 2.0 gm po as single dose	Routine stool for ova and parasites may be negative. Dx may require specimen from small intestine, endoscopy or "string test". Asymptomatic cyst-passers should be rx. Rx relapses with quinacrine.
Isospora belli	Treatment	TMP/SMX 1 double-strength tablet (TMP 160/SMX 800 mg) po qid x 10 days, then bid x 3 weeks	Pyrimethamine 75 mg po qd x 14 days + Folinic acid 10 mg po qd x 14 days	In HIV/AIDS pt, chronic suppressive rx required (<i>NEJM</i> 320:1044, 1989; <i>Ann Int Med</i> 109:474, 1988). Investigational: Diclazuril (R64433 Janssen) 200 mg/d x 7 days. Symptoms decreased in 8/8, stools negative in 8/8 (<i>Lancet</i> 1:1397, 1989).
	Suppression (maintenance rx)	TMP/SMX 1 double-strength tablet 3x/week	Pyrimethamine 25 mg po qd + Folinic acid 5 mg po/day	

Abbreviations: TMP/SMX = trimethoprim/sulfamethoxazole; sc = subcutaneous

TABLE 8 (12)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Parasitic infections — Protozoan infections — Intestinal (continued)				
Microsporidia		There is no standard treatment		Can be detected by light microscopy in stool specimens with modified trichrome stain (<i>NEJM</i> 326:161, 1992). Albendazole available from SmithKline Beecham (1-800-366-8900). Controlled trial in development (ACTG 207). Metronidazole (500 mg po tid) diarrhea ↓ in 10/19 pts, none cleared. Trial of atovaquone in progress.
Enterocytozoon bieneusi	Treatment	There is no standard antimicrobial regimen. Albendazole (200–400 mg po bid for 1 month)		Of 10 pts rx with albendazole: 3 rapid response, 4 no response. Nutritional therapy (low-fat, low-residue diet with simple carbohydrates), 8/9 pts had ↓ stool volume and frequency (<i>Clin Inf Dis</i> 18:819, 1994; <i>J Inf Dis</i> 169:178, 1994).
Septata intestinalis	Treatment	Albendazole (200–400 mg po bid for 1 month)		In one series, 3/3 pts responded to albendazole and diet (<i>Clin Inf Dis</i> 18:819, 1994)
Encephalitozoon helium	Treatment	Not established		Albendazole and itraconazole reported to have efficacy in single case reports (<i>J Infect</i> 27:229, 1993). Ocular lesions have responded to fumagillin eyedrops (<i>Am J Ophth</i> 115:293, 1993).
Parasitic infections — Protozoan — Extraintestinal				
Trichomonas vaginalis		Metronidazole (Flagyl) 2.0 gm po single dose	Metronidazole 0.5 gm po bid x 7 days	Metronidazole contraindicated in 1st trimester of pregnancy; rx with clotrimazole 100 mg vag tabs hs qd x 2 weeks. Cures ~ 20%. ↓ symptoms in most. Rx later with metro, use 7d regimen as blood levels are less. Treat male sexual partners (2.0 gm po as single dose).
Pneumocystis carinii (PCP)	Primary prophylaxis (initiate when CD4 < 200/mm ³ or thrush or unexplained fever)	TMP/SMX 1 double-strength tablet (TMP 160/SMX 800 mg) po qd or 3x/week (see Comments)	Dapsone 100 mg po qd or Pentamidine isethionate 300 mg in 6 ml sterile water by aerosol q4 weeks. For aerosol rx use specific nebulizer (Respi-gard II or System 22 Mizer Jet)	TMP/SMX qd is the recommendation of PHS Task Force on PCP Prophylaxis (<i>MMWR</i> 41:1, 1992). Several recent studies suggest TMP/SMX 1 double-strength tablet 3x/week is as effective with ↓ adverse reactions (<i>Lancet</i> 337:468, 1991). TMP/SMX prophylaxis also ↓ occurrence of Toxoplasma gondii (<i>Am J Med</i> 95:573, 1993). With dapsone, check for G6PD deficiency. Also, the sulfone syndrome reported: fever, rash, hemolytic anemia, atypical lymphocytes and hepatic injury (<i>West J Med</i> 156:303, 1992). Dapsone (100 mg po 2x weekly) has been compared with aerosolized pentamidine (400 mg/month) (2/3 pts had prior PCP), results comparable (<i>AIDS</i> 6:1169, 1992). Low-dose dapsone (100 mg po/week) ineffective. Fansidar ineffective and significant adverse effects. With aerosolized pentamidine, pre-treatment with bronchodilator often needed. Hypersensitivity occurs in both pts and personnel with aerosolized pentamidine. Upper lobe (continued on next page)

Abbreviations: TMP/SMX = trimethoprim/sulfamethoxazole, G6PD = glucose-6-phosphate dehydrogenase

TABLE 8 (13)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Parasitic Infections - Protozoan - Extraintestinal (continued)				
Pneumocystis carinii (PCP) (continued)	Primary prophylaxis (continued)	See previous page	See previous page	(continued from previous page) disease and extrapulmonary dissemination of PCP more common with aerosol pentamidine. Before beginning aerosolized pentamidine rule out pulmonary TB with chest x-ray + 2-3 AFB smears (14% of AIDS pts have TB).
	Treatment Pt NOT acutely ill, able to take oral drugs, $pO_2 > 70$ mmHg	TMP/SMX 2 double-strength tablets po 4x/day (total of 15-20 mg/kg TMP qd) x 21 days or Dapsone 100 mg po qd + Trimethoprim 20 mg/kg qd po divided q6h x 21 days	Clindamycin 600 mg IV q6h x21 days or 450 mg po q6h x21 days + primaquine 15 mg base po qd x 21 days	TMP/SMX and dapsone/TMP equally effective but toxicity ($\uparrow$ LFTs, $\downarrow$ WBC, rash) in 17/30 TMP/SMX vs rash in 9/30 on dapsone/TMP (NEJM 323:776, 1990). If available, monitor serum trimethoprim levels (5-8 μ g/ml desired, Ann Int Med 109:280, 1988). Rarely, dapsone can cause methemoglobinemia. With dapsone and primaquine, check for G6PD deficiency. Regimen useful for patients with severe sulfonamide hypersensitivity. Clinda/primaquine is effective [non-controlled trial, clinda 900 mg IV q8h + primaquine 30 mg po qd, 24/48 episodes treated successfully (Clin Inf Dis 14:183, 1992)]. [Also in small double-blind trial (clinda 600 mg IV q6h x10d then 450 mg po q6h x11d + primaquine 15 mg base po qd x21d), 20/22 response to TMP/SMX and 24/27 to clinda/prima (Clin Inf Dis 17:178, 1993)].
			Atovaquone 750 mg po tid x 21 days	Toxicity low (12%); rash and fever (NEJM 325:1534, 1991). $t_{1/2}$ = 75 hours but given tid. In clinical trial, 31% failure on atovaquone vs 16% on TMP/SMX but atovaquone better tolerated. Follow treatment with 2 ^o prophylaxis (suppression).
	Treatment Pt acutely ill, $pO_2 < 70$ mmHg	Prednisone 40 mg po bid x 5 days, then 40 mg po qd x 5 days, then 20 mg po qd for remainder of anti-PCP rx (11 days). Give 1st dose of prednisone 15-30 minutes before 1st dose of TMP/SMX. + TMP/SMX (20 mg TMP/kg/d) IV divided q6h or q8h x 21 days	Prednisone as in primary + Pentamidine: Isoniazide 4 mg/kg/d IV x 21 days or Trimetrexate 45 mg/M ² IV (over 60-90 min) qd x21 days + leucovorin (folinic acid) 20 mg/M ² IV q6h x24 days (continue 3 days after trimetrexate) or Clindamycin 900 mg IV q8h + primaquine 30 mg po qd	In AIDS patient with PCP and $pO_2 < 70$ mmHg, early treatment with prednisone $\downarrow$ respiratory failure and death ($\uparrow$ herpetic lesions) (NEJM 323:1451, 1990) (do not wait until patient deteriorates further). Initiation of empirical PCP treatment with steroids and TMP/SMX is acceptable BUT it is then essential to establish a diagnosis (BAL, biopsy) within several days since steroids may exacerbate tuberculosis or other pathogens. Steroid rx $\downarrow$ TMP/SMX skin reactions from 11/38 to 3/23 but $\uparrow$ mucocutaneous herpes simplex (Clin Inf Dis 18:319, 1994). Folinic acid may $\downarrow$ toxicity of TMP/SMX but is associated with $\downarrow$ efficacy in rx of PCP. Follow rx with 2 ^o prophylaxis (suppression).
	Suppression	Same as primary prophylaxis (see above)		Without suppressive rx, 60% of HIV+ patients with PCP will relapse within 1 year (MMWR 38:S-5, June 16, 1989).

Abbreviation: AFB = acid-fast bacilli

TABLE 8 (14)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Parasitic Infections - Protozoan - Extraintestinal (continued)				
Toxoplasma gondii	Primary prophylaxis for positive toxo antibody titer (see Comments)	No primary prophylactic treatment has been established as standard-of-care in the U.S.		TMP/SMX when used for P. carinii prophylaxis ↓ toxoplasmosis (Ann Int Med 117:106, 1992; J Inf Dis 169:384, 1994). Trial of clindamycin (300 mg po bid) vs pyrimethamine (25 mg po 3x weekly) vs placebo in U.S. was terminated due to low rate of toxo. After termination, it was observed that mortality on pyrimethamine was 28.9 vs 15.7 on placebo/100 pt years (J Inf Dis 169:384, 1994). Note: pyrimethamine is NOT approved as monotherapy for primary prophylaxis. Two trials are in progress: (1) pyrimethamine 50 mg/week + folinic acid vs placebo (ACTG 154), (2) pyrimethamine 50 mg 1x/week vs 3x/week ± leucovorin. In the pt who cannot take TMP/SMX prophylaxis (for PCP and toxo encephalitis) pyrimethamine 50 mg po + folinic acid 10 mg po is a reasonable alternative (AIDS Clin Care 5:11, 1993). Dapsone (100 mg po 2x weekly) may also be effective as primary prophylaxis (Am J Med 95:573, 1993).
	Treatment (> 90% of pts will respond clinically by 10-14 days; if not, brain biopsy recommended) (See Table 7A, page 22)	Pyrimethamine 200 mg po (loading dose), then 50-75 mg po qd + folinic acid (leucovorin) 10-20 mg po (or IV) qd + sulfadiazine 1.0-1.5 gm po q6h or clindamycin 600 mg po (or IV) q6h for 3-6 weeks	TMP/SMX (5 mg TMP/kg) q6h po or IV for 3-6 weeks or Pyrimethamine + folinic acid (as in primary regimen) + one of the following: Clarithromycin 1.0 gm po q12h or Azithromycin 1.0 gm loading dose, then 0.5 gm po qd or Atovaquone 750 mg po q6h or Dapsone 100 mg po qd	Excellent reference: Wong SV & Remington JS in Textbook of AIDS Medicine; S. Broder, Editor, p. 223, 1993. Also NEJM 329:995, 1993. Use alternative regimen in pts with severe sulfonamide allergy or undertake sulfonamide desensitization (AIDS 5:311, 1991). Pyrimethamine has potential teratogenicity but limited data suggest it can be used in 1st trimester. Trimetrexate + folinic acid not effective as single agent (J Inf Dis 167:1422, 1993). For sulfadiazine, contact CDC ((404) 488-4928)].
	Suppression	Pyrimethamine 50 mg po qd + folinic acid 10 mg po qd + sulfadiazine 1.0 gm po q12h or clindamycin 300 mg po q6h	Pyrimethamine + folinic acid as in primary + azithro or clarithro or dapsone or atovaquone as in treatment	Relapse rate on qd regimen is 5%. A twice/week regimen appears comparable (0/15 relapses). Clindamycin, relapse rate 6%.

TABLE 8 (15)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Parasitic Infections - Protozoan - Extraintestinal (continued)				
Nematode Infections				
Strongyloides stercoralis (strongyloidiasis)		Thiabendazole (Mintezol) 22 mg/kg (maximum 1.5 gm) po q12h x 2 days	Ivermectin 200 µg/kg po qd on days 1, 2, 15 & 16	Retreatment often required. Failures occur with standard thiabendazole (Chest 104:119, 1993). Albendazole (400 mg po q12h x3 d) (not available in U.S.) is better tolerated than thiabendazole. Long-term suppressive rx may be necessary. Response to ivermectin in 7/7 with remissions ≥ 7 months (Clin Inf Dis 17:900, 1993).
Ectoparasites				
Phthirus pubis (crabs)		Permethrin (1% liquid). Wash area, apply lotion for 10 minutes then rinse off	Malathion 5% (Ovid), lindane 1% (Kwell), pyrethrins (Rid), crotamiton (Eurax)	
Scabies (Sarcoptes scabiei)	Norwegian (crusted) scabies seen in immunocompromised pts	Permethrin (5% cream). Thoroughly massage into skin from head to soles of feet. After 8-14 hours, shower to remove.		See Table 7A (Skin) for clinical characteristics. One application of permethrin 5% cream is almost always curative. Lindane may fail and crotamiton not recommended with CD4 < 150/mm ³ .
Viral Infections				
Cytomegalovirus (CMV)	Retinitis Induction and maintenance treatment	Ganciclovir: Induction—5.0 mg/kg IV (infuse at constant rate over 1 hr) q12h x 14-21 days. Maintenance: 6.0 mg/kg IV qd 5 days/week indefinitely or Foscarnet: Induction—60 mg/kg (adjusted for renal function) IV at constant rate (requires infusion pump) over a minimum of 1 hr every 8h for 2-3 weeks. Maintenance—90 mg/kg/day (adjusted for renal function) IV over 2 hrs (requires infusion pump) qd indefinitely (see Comments)	Combination therapy: ganciclovir (5 mg/kg q12h) + foscarnet (60 mg/kg q8h) in patients who failed monotherapy with ganciclovir and/or foscarnet (see Comments)	Both ganciclovir and foscarnet are equally effective in CMV retinitis but in 2 trials [one controlled (ACTG 129), one uncontrolled] median survival was increased in pts on foscarnet (NEJM 326:213, 1992; Am J Med 94:175, 1993). This may reflect the anti-HIV-1 activity of foscarnet. Foscarnet useful in pts with bone marrow suppression from ZDV or other causes. If treatment not followed by chronic suppression, most patients have progressive retinal necrosis within 1 month. Maintenance foscarnet at 120 mg/kg/d (rather than standard 90 mg/kg/d) (adjusted for renal function) resulted in delay in retinitis progression, ↑ survival without substantial ↑ toxicity in 32 pts (J Inf Dis 168:444, 1993). With foscarnet, dose must be ↓ if Cl _{CR} is < 1.5 ml/kg/min (110 ml/min). With ganciclovir, reduction when Cl _{CR} < 80 ml/min (See Table 15, page 94). Adverse effects common with both agents; 36% pts on foscarnet had to be changed to ganciclovir, while 12% on ganciclovir required change to foscarnet (NEJM 326:213, 1992). 9/10 pts who failed monotherapy responded to combination rx. Rate of anemia was ↑ in combination rx but no significant increase in other toxicities (J Inf Dis 167:1184, 1993).

TABLE 8 (16)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Viral infections (continued)				
Cytomegalovirus (CMV) (continued)	Colitis, esophagitis	Foscarnet: see retinitis. Only induction rx used. Dosage reported is 200 mg/kg/d by continuous infusion vs 60 mg/kg q8h as in retinitis. Ganciclovir: see retinitis. Only induction rx used.		Ganciclovir (5 mg/kg IV bid x14 days) resulted in clinical improvement in 12/14 pts with CMV esophagitis but 4/10 relapsed within 3 months (<i>Am J Med</i> 94:446, 1993). Foscarnet (200 mg/kg IV 1x/day x21 days): 11/22 had complete remission 3/17 relapses within 3 months (<i>Am J Gastro</i> 86:876, 1991). Maintenance rx not used but no pts developed CMV retinitis. Long-term remission more likely with CMV esophagitis.
	Hepatitis	Efficacy of agents not established		
	Pneumonia (+ lung biopsy) (See Comments)			CMV often isolated from tracheobronchial secretions without evidence of CMV pneumonitis, hence some authorities suggest that rx not required. In pt with bilateral interstitial pneumonia, intranuclear inclusions, no other pathogens and pt deteriorating, others have treated with ganciclovir (dosage as above) + IV immune globulin (<i>NEJM</i> 324:1005, 1991)
Aphthous ulcers, recurrent	See Table 7A	Topical steroids may ↓ pain and swelling		
Hairy leukoplakia (Epstein Barr virus, EBV)		Usually asymptomatic and no treatment indicated	Acyclovir (800 mg po 5x/d) or topical podophyllin resin (one application) (not currently FDA-approved for this indication)	Patients usually asymptomatic, lesions respond to rx but recur.
Herpes simplex virus (HSV)	Mucocutaneous Treatment	Acyclovir 5.0 mg/kg IV (infuse over 1 hr) q8h x 7 days or 200 mg po 5x/d x 10 days, then:	Foscarnet 40 mg/kg IV (infuse over 2 hrs) q8h x 21 d (pt must be well-hydrated), then:	HSV resistance to acyclovir will occur with high frequency, especially in pts with large ulcers. These respond to foscarnet (<i>J AIDS</i> 7:254, 1994). See package insert for dosage adjustment with ↓ renal function ($Cl_{cr} < 110$ ml/min). Discontinue acyclovir if patient requires ganciclovir.
	Suppression, post-treatment	Acyclovir 400 mg po bid indefinitely	Foscarnet 40 mg/kg IV qd indefinitely	
Human papillomavirus (HPV)	Condyloma acuminatum (CA) (anogenital warts)	Podofilox or 25% podophyllin in tincture of benzoin apply topically, wash after 1–4 hours. Apply weekly x 4. If not ↓, use alternative rx.	Interferon alfa-2b or alfa-n3 1.0 million units (0.1 ml) into lesions 3x/week x 3 weeks. (Only 10 million units/1.0 ml vial is satisfactory. Other concentrations are hypertonic.)	Cervical warts should not be rx until results of Pap smear known. Avoid in pregnant women. Alternatives: cryotherapy with liquid nitrogen, electrocautery. IV 5-fluorouracil may be effective in severe CA.
Molluscum contagiosum virus	Treatment	Usually rx with destructive modalities: cryotherapy with liquid nitrogen, light electrocautery, or curettage.		Alfa interferon is not effective.
	Suppression	Retinoic acid (Retin A) applied once nightly to face may ↓ rate of appearance but does not affect established lesions.		Cannot be used on eyelids or genitalia. Lesions in disseminated cryptococcosis may resemble molluscum contagiosum.

TABLE 8 (17)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS		COMMENTS
		PRIMARY	ALTERNATIVE	
Viral infections (continued)				
Parvovirus B-19	"Pure red cell aplasia"	Immunoglobulin G 0.4 gm/kg IV qd x 5-10 days. Repeat if relapse occurs		Persistent parvovirus B-19 infection is a cause of anemia in HIV+ pts. Rx with IVIG resulted in cure or remission (often prolonged in 6/7 pts) enabling full ZDV dosage (<i>Ann Int Med</i> 113:926, 1990).
Varicella zoster virus (VZV)	Herpes zoster (shingles) Severe: > 1 dermatome, trigeminal nerve, or disseminated	Acyclovir (Zovirax) 10-12 mg/kg IV (infuse over 1 hr) q8h x 7-14 days	Foscarnet 40 mg/kg IV (infuse over 2 hrs) q8h for 14-26 days. See Comments	Treatment must be begun within 72 hours. Chronic post-treatment suppression not required. Acyclovir: adjust dose if renal function ↓. Acyclovir-resistant VZV occurs in HIV pts previously rx with acyclovir. Foscarnet: 4 of 5 pts rx responded, although 2 relapsed within 14 days (<i>Ann Int Med</i> 115:19, 1991; <i>J AIDS</i> 7:254, 1994).
	Not severe	Acyclovir 800 mg po 5 x/day x 7 days		
	Varicella (chickenpox)	Acyclovir 10-12 mg/kg IV (infuse over 1 hr) q8h x 7 days		
Miscellaneous conditions				
Gingivitis (periodontitis/stomatitis) [See Table 7A, page 31]		* Topical Betadine and chlorhexidine gluconate (Peridex) mouthwash + antibiotics effective vs anaerobes (metronidazole, clindamycin or amoxicillin/clavulanate). Often requires curettage debridement.		
Psoriasis	Mild to moderate	Topical steroids + tar		Methotrexate rx has been associated with rapid immune suppression and death (<i>Ann Int Med</i> 106:19, 1987).
	Severe	Skin lesions may improve with zidovudine		
Seborrheic dermatitis	Scalp, mild-moderate	Regular use of dandruff shampoo containing selenium sulfide (Selsun), zinc pyrithione (Head & Shoulders, Danex, Zincon) or sulfur and salicylic acid (Vanseb, Sebulex) + medium potency steroid solution (triamcinolone 0.1%)		Extremely common in HIV+ patients. Involves hairy areas of scalp, face, chest, back and groin.
	Facial, trunk, and/or groin	Topical imidazole cream (ketoconazole 2%, clotrimazole 1%) + low potency topical steroid (hydrocortisone 1-2.5%, desonide 0.05%) applied 2x daily	For refractory trunk lesions, ↑ strength of topical steroid. For severe disease, ketoconazole 200-400 mg po qd x 2-4 weeks	

* This is the regimen used by J.S. Greenspan, *Medical Management of AIDS*, 4th Edition. Eds.: M.A. Sande, P.A. Volberding. W.B. Saunders & Co., 1994

TABLE 9
DRUGS USED IN TREATMENT AND/OR CHRONIC SUPPRESSION OF AIDS-RELATED INFECTIONS:
ADVERSE EFFECTS, COMMENTS, COST

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antibacterial Drugs	Adverse effects on common antibacterial agents such as the penicillins and cephalosporins are not unique in the HIV+ patient. For such information, see GUIDE TO ANTIMICROBIAL THERAPY.
Antifungal Drugs	
Amphotericin B (Fungizone) 0.5-0.8 mg/kg/d IV until response, then 0.8 mg/kg every other day IV. 50 mg \$37.06	Administration of IV amphotericin B has evolved from numerous uncontrolled experiences (<i>AJHP</i> 49:1150, 1992). Before starting, evaluate patient's sodium status (diuretics, Na ⁺ restriction); is the patient also on a Na ⁺ -containing β -lactam antibiotic (ticarcillin, piperacillin, etc.)? What is patient's baseline renal function, cardiac function, hyperkalemia? If patient Na ⁺ -depleted or dehydrated, give 500 ml 0.9% saline IV 30 minutes before starting amphotericin B (<i>Arch Int Med</i> 148:2389, 1988). Manufacturer recommends 1.0 mg test dose (only 20% of pts receive it). There are no data to confirm its necessity. Suspend amphotericin B in 5% D/W (not electrolyte solutions), to concentration 0.1 mg/ml. Premedication with acetaminophen 650 mg po commonly used. Hydrocortisone (25 mg) into IV tubing or in IV ↓ febrile reactions. Severe rigors can be controlled with meperidine (25-50 mg IV). Heparin not needed if given through central line. Rate of administration is controversial, if Cl _{CR} > 25 ml/min and pt not hyperkalemic. Infusion-related toxicity similar with 1-hr and 4-hr infusions (<i>ARC</i> 34:1402, 1992; <i>Am J Med</i> 93:123, 1992). Short infusion facilitates outpatient rx. Other agents used to ↓ infusion toxicity include ibuprofen (others consider it contraindicated), dantrolene to ↓ rigors. In animal model, pentoxifylline ↓ nephrotoxicity (<i>ARC</i> 34:241, 1990). Clinical studies in progress. Following infusion, give another 500 ml 0.9% saline solution. Adverse effects: phlebitis, rigors, fever; GI: nausea, vomiting, anorexia, metallic taste, abdominal pain; Renal: GFR ↓ ~ 40% within 2 weeks, then stabilizes at 20-60% of normal (If Cr ↑ rapidly, interrupt for 2-5 days), nephrocalcinosis, renal tubular acidosis (rare); Electrolytes: hypokalemia, hypomagnesemia. Cardiac: If too rapid infusion, hypotension, ventricular fibrillation, cardiac arrest reported (very rare). Holter monitoring has not shown dysrhythmias with 1-hour infusions (<i>ARC</i> 36:2542, 1992). Blood: anemia (common). Endocrine: ↓ urinary 17-OH corticoids.
Fluconazole (Diflucan) 100-400 mg/d po 100 mg \$6.87, 200 mg \$11.25	Adverse effects: Overall in HIV+ patients 21%, discontinuation rate due to side effects 1.5%. Nausea 3.7%, headache 1.9%, skin rash 1.8%, abdominal pain 1.7%, vomiting 1.7%, diarrhea 1.5%, ↑ SGOT 20%. Rare: severe hepatotoxicity, exfoliative dermatitis, alopecia, seizures, ↓ WBCs, ↓ platelets. Comments: Adverse effects more common in HIV+ patients. No effect on mammalian steroid metabolism. Drug-drug interactions common, see Table 19.
Flucytosine (Ancobon) 37.5 mg/kg q6h po 500 mg \$1.93	Serum levels should be measured when possible. Adverse effects: Overall 30%. GI 6% (diarrhea, anorexia, nausea, vomiting); hematologic 22% [leucopenia, thrombocytopenia, when serum level > 100 µg/ml (esp. in azotemic patients)]; hepatotoxicity (asymptomatic ↑ SGOT, reversible); skin rash 7%; aplastic anemia (rare, 2 or 3 cases). False ↑ in serum creatinine on EKTACHEM analyzer.
Imidazoles, topical: clotrimazole (Lotrimin, Canesten, Mycelex); econazole (Spectazole); miconazole (Micatin, Monistat); butoconazole (Femstat); terconazole (Terazol); tioconazole (Vagistat)	Adverse effects: None of consequence. Local reactions, 0.5-1.5%: mild vaginal or vulvar erythema, burning, pruritus, urticaria, rash. Rarely similar symptoms in sexual partner.
Ketoconazole (Nizoral) 400 mg/d po 200 mg \$2.46	Adverse effects: Overall ~ 5% (more common in HIV+ patients). Nausea, vomiting 3%; abdominal pain 1%; pruritus 1%; headache, dizziness, somnolence, photophobia, hypoesthesia, fever, rash, diarrhea, hepatotoxicity (↑ SGOT 2-5%; very rarely fatal) each < 1%; gynecomastia 3-8%, ↓ testosterone and corticosteroid synthesis, reversible adrenal insufficiency, impotence, ↓ libido, azoospermia (with doses ≥ 800 mg/d), anaphylaxis (after single dose). Comments: Gastric acid required for absorption—cimetidine, antacids block absorption. In achlorhydria, dissolve tablet in 4 ml 0.2N HCl, drink with a straw.
Itraconazole (Sporanox) 200 mg/d po 100 mg \$4.92	Adverse effects: On 400 mg/day po, side effects overall 39%. Discontinuation rate ~ 10%. 3 cases of reversible hepatitis (in 2500 pts). GI: nausea 11%, vomiting 5%, diarrhea 3%. Skin: rash 9%, pruritus 3%. CNS: headache 4%. CV: hypertension 3%. General: edema (mechanism unknown) 4%, fever 3%, fatigue 3%. Lab: ↓ K ⁺ 7%, albuminuria 1%, ↑ LFTs 3%.

* From 1994 Red Book, Medical Economics Data. Price is average wholesale price (AWP)

TABLE 9 (2)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antimycobacterial Drugs:	
FIRST LINE DRUGS	
Isoniazid (INH) (Nydrazid, Laniazid, Teebaconin) 300 mg/d po 300 mg tab \$0.04 100 mg/ml in 10 ml vials (IM (Nydrazid, Apothecon) \$14.63	Adverse effects: Overall ~ 1%. Peripheral neuropathy (< 1.0%); pyridoxine 25 mg daily will ↓ incidence; other neurologic sequelae, convulsions, optic neuritis, toxic encephalopathy, psychosis, muscle twitching, dizziness and alterations of sensorium, coma (all rare); allergic skin rashes, lymphadenopathy and vasculitis (SLE-like syndrome), fever, minor disulfiram-like reaction, flushing after Swiss cheese, hepatitis (children 10% mild ↑ SGOT, normalizes with continued rx, age < 20 yrs rare, 20–34 yrs 0.3%, 35–40 yrs 1.2%, ≥ 50 yrs 2.3%) (also ↑ with daily alcohol); blood dyscrasias (rare); + antinuclear 20%; constipation.
Rifampin (Ritadin, Rimactane, Rifocin) 600 mg/d po 3000 mg cap \$1.55 (IV available, Merrell Dow, 600 mg \$79.38)	Adverse effects: INH/RIF discontinued in ~ 3% for toxicity, the following have been reported: gastrointestinal irritation, drug fever 1%, pruritus with or without skin rash 1%, anaphylactoid reactions in HIV+ pts, mental confusion, thrombocytopenia 1%, leucopenia 1%, hemolytic anemia, pure red cell aplasia (very rare), eosinophilia (rare), transient abnormalities in liver function (SGOT 10% > 100 KU, alk p'tase), jaundice (early onset, 1–3 weeks after start of rx) 1.1%, may be more severe (risk of INH + RIF = 1.6x INH alone). "Flu syndrome" (fever, chills, headache, bone pain), shortness of breath—seen if Rif taken irregularly or if daily dose restarted after an interval of no rx. Interferes with some chemical determinations of bilirubin (false elevation); avoid in 1st trimester of pregnancy; discolors urine, tears, sweat, contact lens an orange-brownish color, induces ↑ hepatic microsomal enzyme activity, resulting in ↑ requirement for coumarin-type anticoagulants, ↑ corticosteroid replacement in Addison's disease. ↓ effectiveness of oral contraceptives with ↑ spotting and pregnancies, ↓ effectiveness of methadone with withdrawal symptoms in addicts, ↑ digoxin dosage, ↑ GI absorption of glucose. Steroid-dependent asthmatics may lose control.
Ethambutol (Myambutol) 15–25 mg/kg/d po 400 mg tab \$1.36	Adverse effects: Optic neuritis with decreased visual acuity, central scotomata, and loss of green and red perception; peripheral neuropathy and headache (~1%), rashes (rare), arthralgia (rare), hyperuricemia (rare). Monthly evaluation of visual acuity, with > 10% loss considered significant; usually reversible if drug discontinued. Anaphylactoid reaction. Comment: Disrupts outer cell membrane in <i>M. avium</i> with ↑ activity to other drugs.
Pyrazinamide (PZA) 25 mg/kg d po 500 mg tab \$0.87	Adverse effects: Arthralgia; hyperuricemia (with or without symptoms); hepatitis (not over 2% if recommended dose not exceeded); gastric irritation; photosensitivity (rare). Serum uric acid if symptomatic gouty attack occurs.
Streptomycin 0.75–1.0 gm/d IM	Adverse effects: Overall 8%. Vestibular dysfunction (vertigo); paresthesias; dizziness and nausea (all less in pts receiving 2–3 doses/week); tinnitus and high frequency loss 1%; nephrotoxicity (rare); peripheral neuropathy (rare); allergic skin rashes 4–5%; drug fever.
SECOND LINE DRUGS Para-aminosalicylic acid (PAS) (Na ⁺ or K ⁺ salt) (Teebacin) 10–12 gm/d po Only available from CDC, (404) 639-8123	Adverse effects: Gastrointestinal irritation 10–15%; goitrogenic action (rare); depressed prothrombin activity (rare); G6PD-mediated hemolytic anemia (rare), drug fever, rashes, hepatitis, myalgia, arthralgia. Retards hepatic enzyme induction, may ↓ INH hepatotoxicity.
Ethionamide (Trecator-SC) 500–1000 mg/d po 250 mg tab \$1.52	Adverse effects: Gastrointestinal irritation (up to 50% on large dose); goiter; peripheral neuropathy (rare); convulsions (rare); changes in affect (rare); difficulty in diabetes control; rashes; hepatitis; purpura; stomatitis; gynecomastia; menstrual irregularity. Give drug with meals or antacids; 50–100 mg pyridoxine per day concomitantly; SGOT monthly. Possibly teratogenic.
Cycloserine (Seromycin) 750–1000 mg/d po 250 mg cap \$3.28	Adverse effects: Convulsions, psychoses (5–10% of those receiving 1.0 gm/day); headache; somnolence; hyperreflexia; increased CSF protein and pressure; contraindicated in epileptics and active alcoholics; 50 mg pyridoxine for every 250 mg cycloserine should be given concomitantly.

* See page 74

TABLE 9 (3)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antimycobacterial Drugs (continued) SECOND LINE DRUGS	
Amikacin (Amikin) 7.5–10 mg/kg/d IV or IM 500 mg vial \$71.40	Adverse effects: Nephrotoxicity, ototoxicity [usually high frequency loss—especially with larger total dose (> 10 gm), longer duration (> 10 days), prior aminoglycosides, peak serum level > 32 µg/ml, trough level > 10 µg/ml], rare eosinophilia, arthralgia, fever, skin rash, probable neuromuscular blockade. All aminoglycosides may cause or ↑ neuromuscular blockade. Use with caution in pts with myasthenia gravis, Parkinsonism, botulism, with neuromuscular blocking drugs (Table 19), or with massive transfusion of citrated blood. Avoid concurrent use with ethacrynic acid, furosemide or methoxyflurane. ? ↑ nephrotoxicity with cis platinum. Comments: With edema, ascites, and/or obesity, base dosage on lean body mass or ideal body weight. Do not give in "heparin lock" without first flushing out.
Capreomycin sulfate (Capastat sulfate) 1.0 gm/d IM 1.0 gm \$20.86	Adverse effects: Nephrotoxicity 36%, ototoxicity (auditory 11%), eosinophilia, leucopenia, skin rash, fever, hypokalemia, neuromuscular blockade. Abnormal liver function tests, ? related.
Thioacetazone (Conteben, TBI, Thioparamizone) (NOT MARKETING IN U.S.) 150 mg/d po	Adverse effects: Common: nausea, vomiting, skin rash, dizziness. Uncommon: bone marrow depression, jaundice 0.2%, and renal toxicity. Marked differences in frequency of side effects between racial groups noted, Asia > Africa. Total incidence 21–38%, ½ in 1st 4 weeks, ½ lasted 6 days or less, ½ mild. Comments: Skin reactions reported in 20% of HIV+ pts. Felt to be responsible for a 3% mortality, raising serious questions as to its use, especially in populations where HIV+ is prevalent (Lancet 1:627, 1991).
Ciofazimine (Lamprene) 50 mg/d po 100 mg \$0.23	Adverse effects: Skin: pigmentation (pink-brownish black) 75–100%, dryness 20%, pruritus 5%. GI: abdominal pain 50% (rarely severe leading to exploratory laparoscopy), splenic infarction (very rare), bowel obstruction (very rare), GI bleeding (very rare). Eye: conjunctival irritation, retinal crystal deposition.
Rifabutin (Mycobutin) 300 mg/d po 150 mg \$3.27	Adverse effects: Discontinuation rate 16%. General: fever 2%. GI: nausea 6%, abdominal pain 4%, diarrhea 3%. CNS: Uveitis (about 1% on 600 mg/d, NEJM 330:438, 1994), insomnia 1%. Skin rash 11%, orange-tan skin pigmentation (pseudojaundice). Discolored (reddish) urine 30%. Lab: ↑ SGOT/SGPT 8%, leucopenia (< 1500, 17%), thrombocytopenia (< 50,000, 5%) (Note: abnormal lab values occurred with equal frequency in placebo-rx pts (except neutropenia) and may be due to disease and/or other drugs).
Ciprofloxacin (Cipro) 750 mg bid po 750 mg tab \$5.25 400 mg IV \$28.81	Adverse effects: Overall 16.5%, 3.5% discontinued secondary to side effects. GI 1.5%: nausea, diarrhea, vomiting, abdominal pain. CNS 0.4%: headache, restlessness, insomnia, nightmares, toxic psychosis (very rare). Skin 0.6%: rash, angioedema. Other more rare (< 1%) include arthralgia, interstitial nephritis. Lab: ↑ SGOT 1.7%, ↑ alk p'tase 0.8%, ↓ WBC 0.4%, ↑ creatinine 1.1%. Safety in children, pregnant women not established, in animal models at 5–16x human dosage, cartilage erosion and arthropathy occurred. Comment: This is not an FDA-approved indication, i.e., use is investigational.
Ofloxacin (Floxin) 400 mg bid po 400 mg tab \$3.50 400 mg IV \$27.60	Adverse effects: Overall 11%, 4% discontinued secondary to side effects. GI: nausea 3%, diarrhea 1%. CNS: insomnia 3%, headache 1%, dizziness 1%. Other uncommon (< 1%) include arthralgia, skin rash, Stevens-Johnson syndrome. Lab: eosinophilia, ↑ SGPT, hematuria. Arthropathy in animal models as above. Comment: This is not an FDA-approved indication, i.e., use is investigational.

TABLE 9 (4)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antimycobacterial Drugs (continued) SECOND LINE DRUGS (CONTINUED)	
Clarithromycin (Biaxin) 500 mg bid po 500 mg \$2.86 (FDA approved for MAC; investigational for other atypical mycobacteria, not effective vs <i>M. tuberculosis</i>)	Adverse effects: Overall ~13%, ~3% discontinued drug secondary to side effects. GI ~13%: diarrhea 3%, nausea 3%, abnormal taste 3%, abdominal pain 2%, dyspepsia 2%. CNS: headache 2%. Lab (each < 1%): ↑ SGOT, alk p'tase, ↓ WBC, ↑ prothrombin time 1%, ↑ BUN 4%, ↑ creatinine < 1%. Should not be used in pregnant women, has demonstrated adverse effects in animals at blood levels 2-17x higher than achieved in humans.
Azithromycin (Zithromax) 500 mg/d po 250 mg \$8.12 (investigational in MAC, <i>T. gondii</i> , not effective vs <i>M. tuberculosis</i>)	Adverse effects: Overall 12%, 0.7% discontinued drug secondary to side effects. GI 12.8%: diarrhea 4%, nausea 3%, abdominal pain 2%, vomiting 1%. CNS 1%, ototoxicity (3/21 pts 30-90 days after 500 mg/d, <i>Lancet</i> 343:241, 1994). Lab: ↑ SGOT 1.5%, WBC ↓ or ↑ 1%, others < 1%. Has not been studied in pregnant women. In rats no embryopathy at dose of 60x human total dose. Comment: This is not an FDA-approved indication, i.e., use is investigational.
Imipenem-cilastatin (Primaxin) 500 mg q6h IV 500 mg \$24.58	Active in vitro vs <i>M. tuberculosis</i> . Being used in some trials. Adverse effects: Local: phlebitis 3%. Hypersensitivity 2.5%: rash, pruritus, eosinophilia < 1%. Blood: + Coombs < 1%, neutropenia < 1%. Renal: oliguria < 0.2%. Hepatic: ↑ SGOT, SGPT, alk p'tase < 1%. CNS (0.2%): confusion, seizures (with 0.5 gm q6h 0.5-1.0% but with 1.0 gm q6h ~10%). GI: nausea 2%, vomiting 2% especially with too rapid IV, diarrhea 3%. Comment: This is not an FDA-approved indication, i.e., use is investigational.
Sparfloxacin (Investigational, Rhone-Poulenc)	The most active of the fluoroquinolones against <i>M. tuberculosis</i> and MAC. Adverse effects (in HIV- pts): GI distress, photosensitivity. Limited compassionate use protocol for multidrug-resistant TB: Dr. Bender (313) 996-7297.
Antiparasitic Drugs	
Atovaquone (Mepron) 750 mg tid po 250 mg \$2.81	Adverse effects: Discontinuation rate 9%. Skin rash 23%, only 4% required discontinuation of rx, pruritus 5%. GI: nausea 21%, diarrhea 19%, vomiting 14%, abdominal pain 4%. CNS: headache 16%, insomnia 10%, dizziness 3%. General: fever 14%. Lab: anemia (Hgb < 8.0 gm/dl, 6%), neutropenia (< 750/mm ³ , 3%), ↑ AST 4%, ↑ amylase 7%.
Clindamycin (Cleocin) 600 mg q6h po or IV 150 mg cap \$0.83 (generic) 600 mg IV \$5.80	Adverse effects: Diarrhea ± <i>C. difficile</i> toxin, nausea, rash, neutropenia, eosinophilia
Dapsone (Dapsone USP) 100 mg qd or 2x weekly po 100 mg \$0.18	Adverse effects: Nausea, vomiting, rash, and oral lesions (<i>Clin Inf Dis</i> 18:630, 1994). Hemolytic anemia if G6PD deficient, methemoglobinemia (usually asymptomatic but if pt has dyspnea, O ₂ saturation disproportionately low to pO ₂ ; check for methemoglobinemia—if > 10-15%, discontinue dapsone). Comment: Usually tolerated even if rash after TMP/SMX.
Iodoquinol (Yodoxin) 650 mg tid po 650 mg \$0.18	Adverse effects: Nausea, abdominal cramps, rash, acne, increase in thyroid size and PBI. Optic atrophy risk if daily dose over 2 gm.

* See page 74

TABLE 9 (5)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antiparasitic Drugs (<i>continued</i>)	
Metronidazole (Flagyl) 500–750 mg bid–tid po 250 mg \$1.26	Adverse effects: GI: nausea, vomiting, metallic taste. Neuro: headache, paresthesias, avoid alcohol during & 48 hours post-rx (disulfiram-like reaction). Dark urine, tears, sweat (harmless).
Paromomycin (Humatin) 500 mg tid po 250 mg \$1.80	Adverse effects: GI: doses of > 3 gm, nausea, abdominal cramps, diarrhea. CNS: vertigo, headache. Skin: rash. Comment: This is an aminoglycoside similar to neomycin ("non-absorbed", ~ 3% of dose is absorbed).
Pentamidine isethionate (IV)(Pentam 300) 4 mg/kg/d IV 300 mg \$98.75	Adverse effects: Hypotension with rapid IV administration, rash, nausea, vomiting, nephrotoxicity, cardiac arrhythmia (ventricular tachycardias including torsade de pointes), neutropenia (15%), thrombocytopenia, pancreatitis, hypocalcemia, hypoglycemia followed by hyperglycemia. Sterile abscesses after IM administration.
Pentamidine (aerosol) (Nebupent) 300 mg/month (prophylaxis) 300 mg \$98.75	Adverse effects: Cough may respond to bronchodilator, upper lobe pneumocystis may occur if given with patient sitting. Comment: Risk of extrapulmonary pneumocystis greater than with systemic prophylaxis.
Primaquine 15 mg (base) qd po 26.3 mg \$0.63	Adverse effects: Hemolytic anemia if G6PD deficient; may cause clinically significant methemoglobinemia.
Pyrimethamine (Daraprim, Malocide) 50–75 mg qd po 25 mg \$0.36 (Leucovorin, tablet 25 mg \$20.03—see Comments)	Adverse effects: Rash, vomiting, diarrhea, xerostomia, megaloblastic anemia, neutropenia, thrombocytopenia. Rarely: headache, insomnia, seizures. Comments: Folinic acid (leucovorin) used to reduce pyrimethamine-induced bone marrow suppression. In vitro and in mice, ZDV antagonizes pyrimethamine.
Sulfadiazine 1.0–1.5 gm q6h po Only available from CDC, see Comments	Adverse effects: Allergic reactions: skin rash, drug fever, pruritus, photosensitization. Periarteritis nodosa and SLE. Stevens-Johnson syndrome, serum sickness syndrome, myocarditis. Neurotoxicity (psychosis, neuritis), hepatic toxicity. Blood dyscrasias, usually agranulocytosis. Crystalluria. Nausea and vomiting, headache, dizziness, lassitude, mental depression, acidosis, sulfhemoglobin. Hemolytic anemia in G6PD deficient and unstable hemoglobins (Hb Zurich). ? teratogenic effects. Should not be used in newborn infants or in women near term. Comment: See page 71 regarding alternative agents if sulfadiazine cannot be obtained. As of December 1992, sulfadiazine and triple sulfa were not available in the U.S. Alternatives recommended for toxoplasmosis. If patient is intolerant of clindamycin, call CDC [(404) 639-4928]; a limited supply is available.
Trimethoprim (Proloprim) 5 mg/kg q6h po 200 mg \$0.25	Adverse effects: Rash, pruritus, marrow suppression rare. Comment: Fewer reactions than TMP/SMX.

* See page 74

TABLE 9 (6)

DRUG NAME, GENERIC (TRADE)/USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Antiparasitic Drugs (continued)	
Trimethoprim (TMP)- sulfamethoxazole (SMX) (Cotrim, Bactrim, Septra) (Dosage depends on indication) 1 double-strength tab (160 TMP/800 mg SMX) \$0.09; 80/400 mg IV \$3.48	Adverse effects: More frequent in HIV-infected patients. Most common are skin rash, fever and bone marrow suppression. Increased incidence of toxicity with serum levels > 200 µg/ml. In pts with PCP treated with steroids, skin reactions ↓ from 47% to 13% (<i>Clin Inf Dis</i> 18:319, 1994). Reactions may be due to direct cytotoxicity of the hydroxylamine of SMX on HIV-infected lymphoblasts rather than due to hypersensitivity (<i>Clin Pharm Therap</i> 55:181, 1994). Hyperkalemia can occur with standard doses, more severe in elderly (<i>Ann Int Med</i> 120:437, 1994). TMP results in ↓ renal K ⁺ excretion similar to amiloride (<i>Ann Int Med</i> 119:296, 1993). Aminotransferase elevations occur. Comment: May be able to "treat through" skin rash.
Trimetrexate 45 mg/M ² qd IV plus leucovorin 20 mg/M ² q6h IV 25 mg \$41.65 (Neutrexin)	Adverse effects: Overall discontinuation rate 10% vs 29% with TMP/SMX. Skin rash 3%, fever 2%. Hematol: neutropenia (< 1000/mm ³) 4%. Hepatic: ↑ AST 3%.
Antiviral Drugs (other than antiretroviral, see Table 6A)	
Acyclovir (Zovirax) Oral: 400–800 mg tid po; IV: 5–10 mg/kg q8h IV 200 mg cap \$0.94, 1000 mg IV \$97.89	Adverse effects (oral dosage): Occasional diarrhea, vertigo, arthralgia. Less frequent: rash, fatigue, insomnia, fever, menstrual abnormalities, acne, sore throat, muscle cramps, lymphadenopathy. Adverse effects (IV dosage): Phlebitis, caustic with vesicular lesions with IV infiltration, CNS: 1% lethargy, tremors, confusion, hallucinations, delirium, seizures, coma. Improve 1–2 weeks after rx. [In an overdose pt, ↓ consciousness occurred 24–48 hrs after peak serum level (<i>Am J Med</i> 94:212, 1993).] Neurotoxicity may clear with hemodialysis (<i>Am J Med Sci</i> 305:36, 1993). Renal: 5% ↑ creatinine, hematuria. With high dose, crystallizes in renal collecting tubules → obstructive uropathy. Hepatic: ↑ SGOT, SGPT. Uncommon: rash, diaphoresis, hypotension, headache, nausea.
Foscarnet (Foscavir) 60 mg/kg q8h IV 6.0 gm \$73.28	Foscarnet is approved (indicated) for rx of CMV retinitis in pts with AIDS. Safety and efficacy has not been established for other CMV infections. Foscarnet is also effective in vitro vs HSV-1, HSV-2 (including acyclovir-resistant mutants), VZV and ganciclovir-resistant CMV. It also inhibits HIV-1. In one study, pts rx with foscarnet had ↑ survival over those rx with ganciclovir (<i>NEJM</i> 326:213, 1992). p24 antigen levels ↓ in AIDS pts rx for CMV retinitis (<i>J Inf Dis</i> 166:607, 1992). The intrinsic antiretroviral activity of foscarnet may have contributed. Must adjust dosage if renal function decreased (see Table 18). Adverse effects: Major clinical toxicity is renal impairment (1% of patients) → ↑ creatinine, proteinuria, nephrogenic diabetes insipidus, ↓ K, ↓ Ca, ↓ Mg. Other: headache, mild (100%); fatigue (100%); nausea (80%); fever (25%). CNS: seizures. Hematol.: ↓ WBC, ↓ Hgb. Hepatic: liver function tests ↑. Neuropathy. Penile ulcers.
Ganciclovir (Cytovene) 5 mg/kg q12h IV 500 mg \$34.80	Adverse effects: Overall 32%. Granulocytopenia 40%, thrombocytopenia 20%, anemia, fever and rash occur. Neutropenia may respond to granulocyte colony stimulating factor (G-CSF or GM-CSF). Comment: Drug should be reconstituted immediately before use and unused portion discarded. Reconstituted solution should not be refrigerated. When administered, an in-line filter is required (0.22 micron preferred; if not available, use 5 micron).
Interferon alfa-2b (Intron a) alfa-n3 (Aferon N) 10 million units \$99.55	Adverse effects (intranasal): Painful. Only 10 million units/1.0 ml vial is satisfactory. Other concentrations are hypertonic. Adverse effects (intravenous dosage): Flu-like: fever 98%, fatigue 89%, myalgia 73%, headache 71%. GI: anorexia 46%, diarrhea 29%. CNS: dizziness 21%. Rash 18%, later psychiatric symptoms, alopecia, ↑ TSH, autoimmune thyroid disorders. Hematol.: ↓ WBC 49%, ↓ Hgb 27%, ↓ platelets 35%.
25% podophyllin in tincture of benzoin (Podocon-25, Pododerm, Podofil) 5 ml \$9.52	Adverse effects: Local reactions: pain, burning, inflammation in 50%. No systemic effects.
Podofilox (Condylox) 3.5 ml \$50.40	

* See page 74

TABLE 10
HIV/AIDS IN WOMEN

I. General Aspects

- A. In 1992, 13.5% of reported cases of AIDS were in women. For women age 25-44 years, HIV disease accounted for 7.3% of all deaths. In blacks for 16.5% (the number two cause of death). Seroprevalence based on neonatal cord blood was 1.5/1000 in 1989. At Boston City Hospital it was 1.8%, increasing to > 3% in 1992.
- B. In 1991-1992, the largest proportionate increase in cases by risk factor was heterosexual contact. In 1993, heterosexual contact was the risk factor in 37% of women with AIDS. Heterosexual contact with a partner with HIV or AIDS whose risk was unreported or unknown accounted for one-half. 50% of women were non-Hispanic black, 24% Hispanic.
- C. Transmission of HIV from men to women occurs more readily than from women to men, with a 4-fold ↑ in one study. Factors reported associated with ↑ risk: genital ulcers, anal intercourse, partner with advanced disease, non-menstrual bleeding, increased number of sexual exposures, oral contraceptives. Factors **not** associated with increased risk: intercourse during menstruation, number of STDs, circumcision status of partners.
- D. Risk after several years of unprotected sex with same infected partner is 10-45%.
- E. Despite these aspects, relatively less is written about women's issues. Only small numbers of women have been included in therapy trials.
- II. Initial Assessment. See Table 5
- III. Clinical Manifestations (*Adapted from Wooley, C., AIDS File 5:2-5, 1993*) (Few clinical studies available to date)
- A. AIDS-defining diagnoses:
- Compared to men, women are more likely to present with
 - Candida esophagitis (30%)
 - Chronic ulcerative herpes simplex (25%)
 - Pneumocystis (22%)
- B. Human papillomavirus:
- Infection prevalence not increased
 - Disease incidence increased! Cervical intraepithelial neoplasia (CIN)
- C. Aggressive course, with high rate of progression to cancer if immunosuppressed
- D. Pap smear recommended annually for HIV+ women. We recommend every 6 months for those with CD4 < 200. Colposcopy recommended for any suspicious lesions. There are no contraindications to standard treatment modalities for CIN.
- E. Recurrent/refractory vaginal candidiasis
- May be early manifestation (CD4 may be > 500)
 - HIV diagnosis often missed because testing not offered
- F. Other conditions
- PID may be more severe, 7-17% require hospitalization
 - Menstrual disorders (41% HIV+ women had menstrual abnormalities vs 24% in case controls) include irregular periods, heavier or scantier periods, early menopausal symptoms, ↑ in premenstrual symptoms
- IV. Natural History. Several studies suggest shortened survival in women even after race, age and risk behavior controlled. 2-year survival in women who received ZDV 33% vs 53% in men. Median survival after an AIDS-defining illness was 13.4 months in women vs 17 months in men.
- V. Family Planning. 85% of women with AIDS are in child-bearing years. Certain contraceptives may pose health hazards for HIV+ women (*from Gibbs G, Zeeman B, p. 467, in HIV Infection, Liberman H, Witzburg RA, 2nd Ed., Little Brown & Co.*)

Method of Contraception	Failure Rate	Risks
Sterilization	0.4	No HIV protection
Oral contraceptive	3	May ↑ disease progression; drug-drug interactions common
IUD	3	↑ risk of PID
Latex condom	12	—
Diaphragm cervical cap	18	Potential vaginal abrasions
Sponge	18-28	Potential vaginal abrasions
Nonoxonyl-9	21	Failure rate, irritation of vaginal mucosa

VI. Treatment Issues

- A. Little clinical data available
- B. Theoretical issues
 - Baseline anemia (iron deficiency)
 - Low mean body weight compared to men
- C. Menstrual dysfunction
 - Amenorrhea should be evaluated, start with pregnancy test
 - Premature menopause occurs frequently, consider hormone replacement therapy
- D. Recommended treatment regimens currently identical for men and women

VII. HIV in Pregnancy

- A. Antepartum Care
 - Obtain CD4 count in each trimester (normal pregnancy causes ↓ in CD4)
 - Obtain alpha fetoprotein test at appropriate gestational age
 - B. Zidovudine Therapy: In ACTG Protocol 076, a zidovudine regimen decreased risk of HIV transmission (mother to infant) from 25.5% to 8.3% ($p < 0.001$) (MMWR 43:285, 1994)
 - The eligibility criteria were:
 1. Patient had not received antiretroviral therapy during current pregnancy
 2. No clinical indications for maternal antiretroviral therapy
 3. CD4 count $> 200/\text{mm}^3$ at initial assessment
 - Zidovudine regimen
 1. Zidovudine 100 mg po 5x/day initiated at 14–34 weeks gestation and continued for remainder of pregnancy
 2. During labor, ZDV 2.0 mg/kg loading dose IV over 1 hour, followed by continuous infusion of 1.0 mg/kg/hour until delivery
 3. ZDV syrup to baby (2 mg/kg/dose q6h) beginning 8–12 hours after delivery, continued for 6 weeks
 - This trial has four limitations:
 1. Efficacy in women with CD4 < 200 or women who had used ZDV for extended periods (ZDV-resistant HIV a concern) was not studied
 2. The independent role of antepartum, intrapartum treatment or treatment of the infant cannot be separated
 3. The risk or benefit of ZDV in 1st trimester was not studied
 4. Long-term side-effects in infants not available
 - Based upon this trial, although ZDV is not currently FDA-approved for this indication, the Public Health Service has provided interim recommendations which essentially are that women who meet the eligibility criteria for ACTG 076 (above) be given the option to elect treatment, recognizing the limitations and risks (MMWR 43:285, 1994).
 - C. PCP prophylaxis: Recommended because PCP in pregnancy may be more severe (perhaps delayed diagnosis)
 - TMP/SMX used although use during last trimester may be associated with ↑ frequency of kernicterus in baby
 - Aerosolized pentamidine, little systemic absorption: distribution unknown when ventilation altered by pregnancy
 - Dapsone: no known adverse effects, but experience limited
-

TABLE 11
ANTIMICROBICS IN PREGNANCY

DRUG	FDA PREGNANCY CATEGORIES*	PLACENTAL TRANSFER (%)	BREAST FEEDING	ADVERSE EFFECTS: FETUS, MOTHER
Antibacterial Agents				
Beta Lactams				
Penicillins	B	10-100	OK	None
Cephalosporins	B	10-40	OK	None
Imipenem/cilastatin	C	?	OK	None
Aminoglycosides:				
Amikacin	D	16	OK	Ototoxicity
Macrolides:				
Erythromycin	B	5-20	OK	None
Azithromycin	B	?	?	None
Clarithromycin	C	?	OK	Fetal toxicity in primates
Clindamycin	-	6-46	OK	None
Fluoroquinolones	C	80-90	No	Potential arthropathy
Metronidazole	B	+	No	None: do not use in 1st trimester
Antifungal Agents:				
Amphotericin B	B	+	OK	None
Fluconazole	C	?	?	NHS
Itraconazole	C	?	No	NHS
Ketoconazole	C	+	No 48 hrs.	NHS
Antiparasitic Agents:				
Pentamidine	C	+	No	NHS
Primaquine	-	+	OK	Hem-G6PD
Pyrimethamine	C	+	? No	None: do not use in 1st trimester
Sulfonamides	C	70-90	No	Potential kernicterus & hem-G6PD
Trimethoprim	C	30-100	OK	None
Antimycobacterial Agents:				
Isoniazid	C	100	OK	None
Rifampin	C	33	OK	Postnatal bleeding in infant
Pyrazinamide	-	?	OK	None
Ethambutol	-	30	OK	None
Streptomycin	D	10-40	OK	Ototoxicity (16% deafness)
Dapsone	C	+	? OK	Hem-G6PD
Antiviral Agents:				
Acyclovir	C	70	OK	None
Didanosine	B	+	?	-
Foscarnet	C	?	?	-
Ganciclovir	C	?	No	Carcinogenic in animals, NHS
Zalcitabine	C	?	?	NHS
Zidovudine	C	100	? No	None

* FDA Pregnancy Categories: A—adequate studies in pregnant women, no risk; B—animal studies no risk, but human studies not adequate or animal toxicity but human studies no risk; C—animal studies show toxicity, human studies inadequate but benefit of use may exceed risk; D—evidence of human risk, but benefits may outweigh; X—fetal abnormalities in humans, risk > benefit.

Abbreviations: Hem-G6PD = hemolysis in individuals with G6PD deficiency; NHS = no controlled human studies

GENERAL:

- In 1993, ~16% of the 103,500 newly reported cases of AIDS in the U.S. were in women, 85% of whom are of child-bearing age.
- Seroprevalence studies based on neonatal cord blood samples (1989) indicated that 1.5/1000 women who gave birth in the U.S. were HIV+. In inner-city hospitals, e.g., Boston City Hospital, the seroprevalence (1992) was > 3%.
- Detection of HIV-infected women, prevention of pregnancy, decreasing transmission to the fetus/infant and early detection and treatment of infected infants are major goals (see Table 10).

TRANSMISSION:¹

- Over 90% of HIV+ children in U.S. acquired their infection from their mothers perinatally: in utero, during delivery, or postpartum through breast feeding. Risk of transmission in Europe 15%, in New York City 28%, in San Francisco 31%.
- Time of transmission:
 - In utero: HIV has been identified in fetal tissues as early as 8 weeks.
 - Intrapartum: at least 1/2 of transmissions believed to occur through exposure to mother's blood or amniotic fluid during delivery.
 - Postpartum acquisition is rare. Only documented cases through breast feeding. Breast-fed infants have an ~14% increased risk of becoming infected. In mothers seroconverting during lactation, the risk is 1/3 (*Lancet* 342:1437, 1993).
- Factors affecting transmission:
 - Stage of infection: risk is 3-fold higher in HIV+ women with CD4 < 400/mm³ compared with women whose CD4 is > 700/mm³.
 - Viremia: risk is ↑ if virus is detectable in peripheral blood.
 - Antigenemia: risk was 29% in women with p24 antigenemia vs 10% in individuals who were p24 antigen negative.
 - Gestational age: infants born at < 33 weeks gestation had infection rate of 33% vs 14% in infants with gestational age > 33 weeks.
- Prevention of transmission
 - Zidovudine for prevention of HIV transmission from mother to infant, see Table 10 for details and recommendations
 - Intrapartum: avoid fetal scalp blood samples and scalp electrodes
 - Avoid breast feeding if safe, adequate bottle feeding is available (*Lancet* 342:1437, 1993)

DIAGNOSIS:

- "All" infants born to HIV-infected women have anti-HIV IgG since IgG crosses placenta at 30-32 weeks or later in gestation. "All" will be ELISA and Western blot positive.
- In infants less than 18 months, diagnosis of HIV infection depends on viral culture, PCR or p24 antigen assay. "Positive" is based on + results from 2 of the 3 methods or one method on 2 occasions. HIV+ infants who do not have definitive virologic diagnosis should have ELISA and Western blot repeated every 3 months (until age 1 year), then at 18 and 24 months of age (*Ped Inf Dis J* 12:513, 1993)
- Definitions for in utero (early) vs intrapartum (late) transmission (*NEJM* 327:1246, 1992)
 - In utero: viral culture and/or PCR+ on blood within 48 hours of birth. (Ideally both cord blood and peripheral blood samples)
 - Intrapartum: diagnostic studies negative during first week but + from days 7-90 and infant not breast-fed
- Current research approaches:
 - Anti-HIV IgA: IgA does not cross placenta. Reliability not yet established.
 - Immune complex dissociated (acid-dissociated) HIV p24 antigen assay: standard p24 assay in newborns is unreliable since circulating antigen is complexed to maternal antibody and is undetectable. Technique identified 7/7 HIV-positive and 22/22 HIV-negative infants (*NEJM* 328:297, 1993).
 - bDNA assay may be useful, but data on efficacy not available (see Table 2).

¹ From Pediatric AIDS: Part II, D. Wara, *AIDS Clin Care* 5:21, 1993

NATURAL HISTORY:

- Untreated (no antiretroviral rx and no PCP prophylaxis): Symptomatic disease occurred at median age 8 months, 80% infants symptomatic by age 2. Median survival 38 months (*NEJM* 321:1791, 1989). In children with minimal complications at diagnosis of AIDS median survival 66 months, whereas with serious complications at diagnosis median survival 9 months (*Ped Inf Dis J* 12:310, 1993). The rate of disease progression in infants is directly related to the severity of maternal disease at time of delivery (*NEJM* 330:308, 1994).
- Treated: Perinatally infected children who receive ZDV at onset of symptoms, median survival 7-8 years (*Lancet* 339:449, 1992; *AIDS Clin Care* 5:48, 1993).

TABLE 12B
CDC CLASSIFICATION SYSTEM FOR HIV IN CHILDREN*

CLASS P-0. INDETERMINATE INFECTION

Infants < 15 months born to infected mothers but without definitive evidence of HIV infection or AIDS.

CLASS P-1. ASYMPTOMATIC INFECTION

Subclass A. *Normal immune function*

Subclass B. *Abnormal immune function*: hypergammaglobulinemia, T4 lymphopenia, decreased T4:T8 ratio, or absolute lymphopenia

Subclass C. *Immune function not tested*

CLASS P-2. SYMPTOMATIC INFECTION

Subclass A. *Nonspecific findings* (≥ 2 for ≥ 2 months): fever, failure to thrive, generalized lymphadenopathy, hepatomegaly, splenomegaly, enlarged parotid glands, persistent or recurrent diarrhea

Subclass B. *Progressive neurologic disease*: loss of developmental milestones or intellectual ability, impaired brain growth, or progressive symmetrical motor deficits

Subclass C. *Lymphoid interstitial pneumonitis*

Subclass D. *Secondary infectious diseases*

Category D-1. *Opportunistic infections in the CDC case definition*

Bacterial: mycobacterial infection (non-cutaneous, extrapulmonary, or disseminated)

Fungal: candidiasis (esophageal, bronchial, or pulmonary), coccidioidomycosis, disseminated histoplasmosis, extrapulmonary cryptococcosis

Parasitic: *Pneumocystis carinii* pneumonia, disseminated toxoplasmosis with onset ≥ 1 month of age), chronic cryptosporidiosis or isosporiasis, extraintestinal strongyloidiasis

Viral: cytomegalovirus disease (onset ≥ 1 month of age), chronic mucocutaneous/disseminated herpes (onset ≥ 1 month of age), progressive multifocal leukoencephalopathy

Category D-2. *Unexplained, recurrent, serious bacterial infections* (2 or more in a 2-year period): sepsis, meningitis, pneumonia, abscess of an internal organ, bone/joint infections

Category D-3. *Other infectious diseases*: including persistent oral candidiasis, recurrent herpes stomatitis (≥ 2 episodes in 1 year), multidermatomal or disseminated herpes zoster

Subclass E. *Secondary cancers*

Category E-1. *Cancers in the AIDS case definition*: Kaposi's sarcoma, B-cell non-Hodgkin's lymphoma, or primary lymphoma of brain

Category E-2. *Other malignancies possibly associated with HIV*

Subclass F. *Other conditions possibly due to HIV infection*: including hepatitis, cardiopathy, nephropathy, hematologic disorders, dermatologic diseases

* Age 12 years or less. This classification is currently under revision (May 1994).

INITIATION OF ANTIRETROVIRAL THERAPY, P. CARINII PROPHYLAXIS, AND SUPPORTIVE THERAPY

(*Ped Inf Dis J* 12:513, 1993; *Am Acad Ped Red Book*, 1994)

A. P. carinii Prophylaxis

1. P. carinii pneumonia (PCP) can occur early in life, before a "confirmed positive" diagnosis of HIV infection can be established, page 83. Infants born to HIV+ mothers should have CD4 counts performed at birth and every 3 months until age 2.
2. PCP prophylaxis should be started for any child with an episode of PCP or CD4 counts (%) below age-adjusted values:

Age	CD4 Cell Criteria (cells/mm ³ —%)	
	PCP Prophylaxis	Antiretroviral Rx
< 1 year	< 1500 (<20%)	< 1750 (<30%)
1–2 years	< 750 (<20%)	< 1000 (<25%)
2–6 years	< 500 (<20%)	< 750 (<20%)
> 6 years	< 200 (<20%)	< 500 (<20%)

3. PCP prophylaxis should be discontinued for children proven not to be HIV-infected (> 24 months of age).

B. Antiretroviral Therapy

1. Indicated for children with a definitive (positive) diagnosis of HIV infection **and** who have: (a) evidence of significant immunodeficiency (decreased CD4 counts) or (b) HIV-associated clinical criteria regardless of CD4 count. Routine antiretroviral rx is **not** recommended for asymptomatic children with normal immune status; lymphadenopathy, hepatomegaly or hypergammaglobulinemia as only findings are considered asymptomatic (*Ped Inf Dis J* 12:513, 1993).
2. Clinical criteria (definite indications, independent of CD4 count)
 - a. An AIDS-defining infection, Class P-2, Category D-1 (see above, Table 12B)
 - b. Wasting or failure to thrive (children who cross 2 percentiles or are below 5th percentile for age of standard growth curves)
 - c. Progressive encephalopathy attributable to HIV
 - d. AIDS-associated malignancy, Category E-1
 - e. Two or more episodes of septicemia or meningitis, Category D-2
 - f. Thrombocytopenia (platelet count < 75,000/mm³ on 2 or more occasions over a 2-week period)
 - g. Hypogammaglobulinemia (total Ig level < 250 mg/dl)
3. Clinical criteria (possible indications, independent of CD4 count; these require more clinical judgment): Lymphoid interstitial pneumonitis and/or parotitis; splenomegaly; oral candidiasis that persists > 1 month or is recurrent despite rx; diarrhea otherwise unexplained or persistent (≥ 3 loose stools/day for ≥ 2 weeks) or recurrent (≥ 2 episodes with dehydration in 2 months); symptomatic cardiomyopathy; nephrotic syndrome; transaminase > 5x normal (other etiologies excluded); chronic bacterial infections (sinusitis, pneumonia); ≥ 2 episodes of H. simplex or varicella-zoster in 1 year; neutropenia (< 750/mm³) or age-corrected anemia on 2 occasions over 1 week.
4. Choice of Initial Drug and Regimen
 - a. Zidovudine (The Working Group on Antiretroviral Therapy: National Pediatric HIV Resource Center recommends usage from birth onward, FDA-approved labeling is > 3 months):
 - (1) Age 0–2 weeks 2 mg/kg po q6h
2–4 weeks 3 mg/kg po q6h
4 weeks–13 years 180 mg/M² po q6h
 - (2) If child unable to take anything by mouth for > 48 hours, give 120 mg/M² IV q6h
 - (3) When dose has to be $\downarrow$ because of toxicity, minimal acceptable dose is 75 mg/M² po q6h
5. Indications for Alternative Antiretroviral Therapy
 - a. Zidovudine Failure [progression (usually growth failure or progressive CNS disease) in adherent patient treated for 4–6 months]
 - (1) Growth failure: moving downward > 2 percentile lines from established curve on 2 consecutive monthly measurements, or sustained deviation from a parallel curve for children below 5th percentile
 - (2) Progressive CNS disease (see *Ped Inf Dis J* 12:513, 1993, Table 4)
 - b. Zidovudine Intolerance
 - (1) Hemoglobin (< 8.0 g/dl). $\downarrow$ dose of ZDV by 30%. If Hgb remains < 8.0 g/dl, give erythropoietin. If Hgb remains < 8.0, consider alternative agent.
 - (2) Absolute neutrophils < 500/mm³, discontinue ZDV. Also discontinue TMP/SMX, and use dapsone for PCP. If WBC returns to > 500/mm³, restart ZDV at 120 mg/M² q6h. If WBC remains < 500/mm³, give G-CSF.
6. Alternative Therapy
 - a. Didanosine (ddI) (only approved alternative for children): 90–135 mg/M² po q12h. Side-effects include pancreatitis (5%).
 - b. Zalcitabine (ddC) (not approved in children, data are limited): 0.01 mg/kg po q8h. Side-effects: peripheral neuropathy not seen in children.

C. Supportive Treatment and Prophylaxis

1. Intravenous immune globulin (IVIG)

- a. Recommended for infants and children with evidence of humoral immune defects (hypogammaglobulinemia or significant recurrent infections despite antimicrobial therapy. IVIG 400 mg/kg q28 days is recommended. Ages and "normal" Ig ranges (mg/dl) (*Pediatrics* 37:715, 1966):

Age	Newborn	1-3 months	4-6 months	7-12 months	13-24 months	2-3 years	3-5 years	6-8 years
Ig	1044±201	481±127	498±204	752±242	870±258	1024±205	1078±24	1112±293

- b. Thrombocytopenia ($< 20,000/\text{mm}^3$) on ZDV: IVIG 0.5-1.0 g/kg/dose x 3-5 days

2. Immunization: See Table 12F, page 91

3. *Mycobacterium avium* complex: prophylaxis recommended in adolescents, see Table 8, page 59. Recommendations have not been made for infants and children.

4. Psychosocial support (see *Am Acad Pediatrics, Red Book, 1994*): School attendance, child/foster care, adolescent education

TABLE 12D
CLINICAL SYNDROMES, OPPORTUNISTIC INFECTIONS, IN INFANTS AND CHILDREN, COMPARISON WITH ADULTS*

CLINICAL SYNDROME	INFANT/CHILD	ADULT	CLINICAL FEATURES (in children)/COMMENTS
Central Nervous System			
Encephalopathy Static course	Common	0	25% children show cognitive and motor deficits. Most have head circumference in 10-25th percentile. Problems with verbal expression, attention deficits, hyperactivity. Mild ↑ reflexes in legs to spastic diplegia. IQ stable.
Plateau course	Uncommon	0	Infant's or child's gain of cognitive or motor skills plateaus. Motor deficits are common. IQ usually only 50-79.
Subacute progressive course	Uncommon	AIDS dementia common	Gradual progressive decline in motor, language, adaptive function. Early, child is alert, wide-eyed, with a paucity of facial movements. Endstage: mute, dull-eyed, quadriparetic. CSF: mild pleocytosis, ↑ protein, may be + for HIV antibody and virus. CT: atrophy, progressive calcification in basal ganglia (most common in infants and young children).
Focal brain diseases: seizures, focal neurologic deficits Primary CNS lymphoma	Uncommon	Uncommon	Uncommon but the most common cause of mass lesion in children. Clinical: seizures, hemiparesis, memory loss. CT: lesion usually solitary, > 3 cm, variable contrast enhancement, no response to antitoxo rx.
Cerebrovascular event	Rare	Rare	True incidence unknown, but occurs. Occurs most often with immune-mediated thrombocytopenia.
Infections Toxoplasmosis	V. rare	Common	Toxo is uncommon since it is most often due to reactivation.
Progressive multifocal leuco-encephalopathy (JC virus)	V. rare	V. rare	PML is uncommon since it is most often due to reactivation.
Bacterial meningitis	No increase in HIV+		Initial reports identified cases including 2 cases of late onset group B strep meningitis (3½ and 5 months) but subsequently frequency does not seem increased.
Myelopathy, diffuse Vacuolar myelopathy	V. rare	Rare	Seen in 2/40 patients in an autopsy series (<i>Ped Path</i> 10:155, 1990).
Endocrine			
Failure to thrive and growth retardation	Common	Wasting syndrome common	33/36 HIV+ children showed failure to thrive, not purely related to diarrhea and malnutrition. Known causes of growth failure are growth hormone deficiency, hypothyroidism, and glucocorticoid excess. None of these has been seen with any frequency in HIV+ children.
Eye			
Cytomegalovirus retinitis	Uncommon	Common	CMV chorioretinitis in 1.6% children vs 10-20% in adults (<i>Arch Ophthal</i> 107:978, 1989). In children it usually occurs with generalized CMV infection, viremia and multiple organ involvement. When present, ocular lesions are same as in adults, Table 7, page 28.
Retinal depigmentation, on ZDV	~ 5%	0	Asymptomatic peripheral retinal depigmentation (dosages > 300 mg/M ² /d)
HIV-associated "cotton wool" spots	Rare	Common	Seen only in children > 8-10 years, while seen in 60-70% of adults.
Gastrointestinal Tract			
Mouth Thrush (candidiasis)	Common	Common	Oral candidiasis occurs in 15-40% HIV-infected children. Clinically similar to adults, Table 7, page 30.

* Most of the information in this table has been obtained from *Pediatric AIDS, 2nd Ed.*, Eds. P.A. Pizzo, C.M. Wilfert, Williams & Wilkins, 1994.

TABLE 12D (2)

CLINICAL SYNDROME	INFANT/CHILD	ADULT	CLINICAL FEATURES (in children)/COMMENTS
Gastrointestinal Tract (<i>continued</i>)			
Mouth (<i>continued</i>)			
Herpes simplex virus	Common	Common	Prolonged fever, deep chronic ulceration, frequent recurrences in 5–10% of children. HSV lesions > 28 days are AIDS-defining illness. Disseminated HSV is rare. Rx with acyclovir.
Kaposi's sarcoma	V. rare	Common	21 cases have been reported. Clinical spectrum similar to adults.
Esophagus			
Dysphagia, odynophagia	Uncommon	Common	When pain/difficulty occur, children more likely to refuse to eat. CMV—odynophagia, Candida—dysphagia.
Small bowel/colon			
Acute diarrhea, failure to thrive, chronic diarrhea	Common	Common	Etiologies in children probably the same as in adults but studies specifically in children are lacking. Lymphoid hyperplasia (~ to LIP) seen with diarrhea but no pathogens.
GI bleeding	Uncommon	Uncommon	CMV is prime suspect.
Heart	Common	Common	Abnormal ECG changes (ventricular hypertrophy and non-specific ST-T changes) in 55–93% HIV+ children.
Cardiomyopathy	Common	Uncommon	Left ventricular dysfunction 29–74% (most important cardiac change). 20% transient or chronic congestive failure. Unexpected cardiorespiratory arrests in 8/81 (<i>JAMA</i> 269:2869, 1993).
Hematologic Abnormalities			
Anemia	Common	Common	20% of untreated symptomatic children have hemoglobin < 10 gm/dl.
Leucopenia (< 3000/mm ³)	Common	Common	38% of untreated symptomatic children. Lymphopenia less common than in adults.
HIV-related immune thrombocytopenia	Common	Common	May be initial manifestation of disease, preceding other symptoms by several years. Rx has included antiretroviral agents, IVIG, steroids and rarely splenectomy.
Drug-related	Common	Common	Myelosuppression is major ZDV toxicity. Didanosine associated with granulocytopenia (< 1000/mm ³) in 24% children, anemia and thrombocytopenia < 5%.
Hepatobiliary	Rare	Common	Very few reports relating to children. Etiologies such as AIDS cholangiopathy, peliosis hepatis (bacillary angiomatosis) not reported. 2 cases of fatal hepatic necrosis associated with adenovirus reported (<i>Rev Inf Dis</i> 12:303, 1990).
Lung			
Pneumocystis carinii	Common	Common	PCP when it occurs, 72% children < 1 year, 38% in older children. Clinical: Fever, cough, tachypnea, hypoxia. X-ray: Diffuse bilateral interstitial pattern; less often, no infiltrate, cysts, nodules, unilateral or focal infiltration or "white-out".
Bacterial pneumonia: Strep. pneumoniae most common, Haemophilus influenzae b (less common)	Common	Common	18% of HIV+ children followed 12 months developed pneumonia. Clinical: fever, cough, tachypnea, diminished breath sounds, wet rales. X-ray: usually localized with alveolar pattern. Pleural effusion supports dx. Lab: leucocytosis, ↑ PMNs common. Blood cultures, antigen in blood/urine.
Viral pneumonia: Respiratory syncytial virus	Uncommon	Rare	Clinical presentation unremarkable except wheezing in 1/10 in 1 series (<i>J Ped</i> 117:251, 1990), generally unresponsive to ribavirin.
Tuberculosis	Uncommon	Common	Only a few cases reported in children. Clinical: fever, cough. X-ray: often focal infiltrates with hilar adenopathy, cavitation uncommon.
Fungal: histoplasmosis, coccidioidomycosis	Uncommon	Uncommon	Only isolated single case reports.
Cytomegalovirus pneumonia	Uncommon	Uncommon	Dx of CMV pneumonia is problematic. See Table 7, page 46. Clinical: progressive dyspnea, non-productive cough, tachypnea usually of gradual onset, mild to moderate hypoxemia. Diffuse interstitial pattern.

TABLE 12D (3)

CLINICAL SYNDROME	INFANT/CHILD	ADULT	CLINICAL FEATURES (in children)/COMMENTS
Lung (continued) Lymphocytic interstitial pneumonitis (LIP)	Common	V. rare	LIP occurs in 40% of children with perinatally acquired HIV. HIV and EBV antigens have been demonstrated in lung tissue. Usually diagnosed in children > 1 year vs PCP which is common in first year. Clinical: slowly progressive tachypnea, cough, wheezing, hypoxemia. Rales are infrequent. Clubbing of digits is characteristic. Generalized lymphadenopathy, hepatosplenomegaly and parotid swelling. X-ray: diffuse interstitial. Bacterial superinfection is common. Diagnosis by lung biopsy. Rx: steroids may be of some benefit.
Congestive heart failure	Common	Uncommon	See Heart, above
Musculoskeletal Drug-associated myopathy	Rare	Uncommon	Two children with zidovudine-associated myopathy reported. See Table 7, page 48 for myopathy in adults.
Pyomyositis	Rare	Rare	Two cases reported in children.
Renal Nephropathy	Common	Rare	Nephropathy observed in 29% children with perinatal AIDS (Kidney 31:1167, 1987). In children may present with nephrotic syndrome with a course of 12-18 months (NEJM 321:625, 1989). Steroid rx may be of value.
"Sepsis"	Common	Uncommon	25% of symptomatic HIV+ children will have bacteremic episodes, most due to bacteremic pneumonia or bacteremia without a focus (Pediatric AIDS, Eds. P.A. Pizzo, C.M. Wilfert, Ch. 13, page 199, 1991).
Sinuses	Common	Common	In children with serious bacterial infections, sinusitis was 3rd behind pneumonia and sepsis.
Skin Impetigo	Common	Uncommon	Due to Staph. aureus or Group A strep. Clinical: areas of erythema with "honey crusting." May be widespread and evolve into "cellulitis."
Oral thrush	Common	Common	See GI, mouth above. Poor response to topical therapy may be noted.
Monilial diaper "rash"	Common		Lesions widespread, rapid recurrence after rx stopped.
Tinea capitis	Common		May extend to face. Requires griseofulvin but often recurs after rx.
Herpes simplex virus	Common	Common	Severe and persistent infection of oral mucosa, fingers, or other skin surface.
Varicella zoster virus	Common	Common	Rare in healthy children, can be a presenting sign of HIV disease. Lesions tend to be more severe and painful, heal with scarring and recur. Rx: acyclovir.
Papillomavirus (warts)	Common	Common	Lesions may be widespread and persistent. Condyloma acuminatum can occur.
Scabies, Norwegian	Uncommon	Uncommon	See Table 7, page 51
Molluscum contagiosum	Common	Common	Lesions may be large and widespread.
Vasculitis	Rare	Rare	Chronic leukocytoclastic vasculitis reported; may be caused by HIV or zidovudine.
Drug eruptions	Common	Common	Incidence increased in HIV+ children. On TMP/SMX 16% developed rashes. Stevens-Johnson syndrome and toxic epidermal necrolysis reported with TMP/SMX and anti-TB drugs.
Malassezia furfur folliculitis	Uncommon	Rare	Pruritic, papular eruption on face and neck. Fungemia not reported.

Abbreviation: TMP/SMX = trimethoprim/sulfamethoxazole

TABLE 12E
DRUGS FOR TREATMENT OF CHILDREN: DOSAGE, ROUTE, COMMENTS*

INDICATION	DRUG	DOSAGE	FORMULATIONS	COMMENTS
HIV-1	Zalcitabine (ddC)	0.005 or 0.01 mg/kg po q8h		In clinical trial
	Didanosine (ddI)	90–100 mg/M ² po q12h (see package labeling for detailed dosing). Take 2 hrs after or 1 hr before meals or other medication to minimize interactions	• Mint-flavored chewable/dispersible buffered tablets • Pediatric powder for oral solution (2 or 4 gm/bottle)	See Table 12C
	Zidovudine (ZDV)	180 mg/M ² po q6h See Table 12C	• Raspberry flavored syrup (50 mg/5 ml) • Capsules (100 mg) • IV	See Table 6A for toxicity
Antiparasitic Drugs				
<i>P. carinii</i> Prophylaxis	TMP/SMX or Dapsone or Aerosolized pentamidine	150 mg/M ² TMP component po divided bid on 3 consecutive days (M, T, W) each week 1 mg/kg/day po (not to exceed 100 mg)	Oral suspension (cherry or grape flavored) No pediatric formulation	
	Treatment			
	TMP/SMX	Children > 2 months 20 mg TMP/100 mg SMX/kg/d divided q6h po or IV in same dose q6–8h		
	Pentamidine isethionate	4 mg/kg/d IM x12–14 d		
Antifungal Drugs				
	Amphotericin B	0.25–1.0 mg/kg/d IV (Same as adult, see Table 6)		
	Fluconazole	6 mg/kg po qd	No pediatric formulation	Optimal dosage not defined
	Itraconazole	3–5 mg/kg po qd		
Antimycobacterial Drugs				
<i>M. tuberculosis</i>	Isoniazid	Neonates: 10 mg/kg po qd. Infants/Children: 10–14 mg/kg po qd (maximum 300 mg/day)	No pediatric formulation	
	Rifampin	10–20 mg/kg po qd (maximum 600 mg/day)	No pediatric formulation	
	Ethambutol	—		Not recommended in children < 13 yrs
	Pyrazinamide	15–30 mg/kg po qd as 1 or more doses (maximum 2.0 gm/day)	No pediatric formulation	
	Streptomycin	20–30 mg/kg IM qd, divided q12h (maximum 2.0 gm/day)		
MAI	Rifabutin	75 mg/d po	No pediatric formulation	Used vs MAI in a 2-year-old
	Clarithromycin	15 mg/kg/d divided q12h po	Pediatric formulation anticipated in mid-1994	No reported experience
Antiviral Drugs				
Herpes simplex virus	Acyclovir	250 mg/M ² IV q8h. Infuse over 1 hour	Oral suspension (banana flavored) available if appropriate	Daily urine output should be 1 ml/1.3 mg of acyclovir
Varicella zoster	Acyclovir	500 mg/M ² IV q8h		
Cytomegalovirus	Ganciclovir Induction	2.5 mg/kg IV q8h		Has potential carcinogenicity. 2 children responded, 2 did not.
	Maintenance	5.0 mg/kg IV q12h		
	Foscarnet	—		No experience in children

* See Tables 6 and 9, for adverse effects and expanded comments. See Table 4A, pages 13–14 for clinical trials actively recruiting children.

TABLE 12F
RECOMMENDATIONS FOR ROUTINE IMMUNIZATION OF HIV+ CHILDREN (ASYMPTOMATIC AND SYMPTOMATIC)

(From Am Acad Pediatrics "Red Book" 1994, pp 23, 264)

VACCINE**	AGE/ROUTE	
Hepatitis B	Birth, 1-2 months	IM
Diphtheria, tetanus, pertussis (DTP)	2, 4, 6, 15-18 months, 4-6 years	IM
Inactivated polio vaccine (IPV)*	2, 4, 15-18 months	SC
Measles, mumps, rubella—live attenuated (MMR)	15 months	SC
Conjugated Haemophilus influenzae b§	2 months	IM
Pneumococcal polysaccharide vaccine	24 months	IM or SC
Influenza vaccine	6 months	IM

* Oral polio vaccine (OPV, live attenuated) has been given to asymptomatic HIV+ children without adverse effects but because family members may be immunocompromised and are at risk for vaccine-associated paralytic polio, IPV is recommended.

** BCG is not recommended in the U.S. However, in areas with high incidence of tuberculosis, WHO recommends BCG immunization of asymptomatic HIV+ children.

§ Vaccination schedule of Haemophilus b conjugate vaccines (MMWR 42:RR-13, Sept. 17, 1993):

VACCINE	AGE AT 1st DOSE (months)	PRIMARY SERIES	BOOSTER
HbOC (HibTITER, Lederle/Praxis)	2-6	3 doses, 2 months apart	At 15 months
	7-11	2 doses, 2 months apart	At 15 months
	12-14	1 dose	2 months later
	15-59	1 dose	
PRP-OMP (PedvaxHIB, Merck)	2-11	2 doses, 2 months apart	At 12 months
	12-14	1 dose	2 months later
	15-59	1 dose	
PRP-D (ProHIBIT, Connaught)	15-59	1 dose	
PRP-T (Act Hib, Smith-Kline Beecham; Omni Hib, Pasteur-Merieux)	2	3 doses, 2 months apart	At 15 months
DTP + HbOC (Tetramune, Lederle/Praxis)	2	3 doses: at 2, 4 and 6 months	At 15 months

TABLE 13
IMMUNIZATION OF HIV+ ADULTS (ASYMPTOMATIC AND SYMPTOMATIC)

General Principles/Guidelines:

- Administration of live attenuated vaccines is contraindicated in individuals with advanced HIV infection (AIDS) (MMR is an exception).
- Immunization with killed whole cell vaccines and/or purified antigens should be done as soon as reasonable after HIV infection diagnosed, before CD4 cells ↓ further.
- Extended primary series and/or more frequent boosters often indicated.
- When specifically indicated, immune globulin (IG) and specific immune globulins can be administered.

RECOMMENDATIONS FOR ROUTINE IMMUNIZATION OF HIV+ ADULTS (United States)
(From Update on Adult Immunization, Centers for Disease Control, MMWR 40:RR-12, 1991, Nov. 15)

VACCINE/TOXOID	STAGE OF HIV INFECTION		BOOSTER DOSE
	ASYMPTOMATIC HIV+*	SYMPTOMATIC (AIDS)*	
Td (tetanus/diphtheria)	Yes	Yes	10 yrs
MMR (measles, mumps, rubella)	Yes	Yes	None
HbCV (Haemophilus influenzae type b conjugate vaccine)	Yes	Yes	None
Pneumococcal	Yes	Yes	6 yrs

(Continued on next page)

VACCINE/TOXOID	STAGE OF HIV INFECTION		BOOSTER DOSE
	ASYMPTOMATIC HIV+*	SYMPTOMATIC (AIDS)*	
Influenza	Yes	Yes	Annual
HBV (Hepatitis B)	(Yes)**	(Yes)**	None
elPV (polio)	(Yes)**	(Yes)**	(None)

Abbreviations: Td = tetanus and diphtheria toxoids, adsorbed (for adult use); MMR = measles, mumps and rubella vaccine; HbCV = Haemophilus influenzae type b conjugate vaccine; Pneumococcal = pneumococcal polysaccharide (23 component) vaccine; HBV = Hepatitis B vaccine; elPV = enhanced-potency inactivated polio vaccine

* Asymptomatic—CDC category A1, A2/Walter Reed Stages 1–4; Symptomatic—CDC A3, B1–3, C1–3/WR Stages 5–6 (see Table 3). ** See Comments

COMMENTS ON "ROUTINE" VACCINES/TOXOIDS*

VACCINE/TOXOID	COMMENTS
Td	"injection" drug users at ↑ risk of tetanus
MMR	Recent reports suggest that measles in HIV+ may be atypical (no rash 1/3) or typical (2/3), that pneumonitis is common (~80%) and fatality high (1/3) (JAMA 267:1237, 1992). In patients born in 1957 or later, although MMR is a live vaccine, adverse effects beyond those in HIV-negative patients have not been reported.
HbCV	Is of unproven benefit and immune responses ↓, but the risk of H. influenzae type b disease is ↑ and adverse reactions are minimal, hence it is recommended.
Pneumococcal	Risk of bacteremia is ↑ [as high as 9.4/1000/yr (J Inf Dis 162:1012, 1990)]. Revaccination 6 years after 1st dose is recommended.
Hepatitis A	In the past several years hepatitis A has ↑ in frequency in homosexual men in the U.S., Canada and Australia (MMWR 45:155, 1992). Outbreaks have also been reported in parenteral drug users (Am J Pub Health 79:463, 1989). < 10% U.S.-born young adults have antibody (Mil Med 157:579, 1992). With the likely licensure of an inactivated hepatitis A vaccine, in 1994, its use in asymptomatic HIV+ and possibly in symptomatic HIV+ individuals would seem appropriate (the ACIP has not made recommendations, 6/1/94).
Hepatitis B	If lifestyle or occupation was risk factor for HIV it is also a risk factor for hepatitis B. Series of 3 IM injections (not into the buttocks) should be given. Test for antibody to HBs Ag 1–6 months after completing series. If anti-HBs is < 10 milli-international units, revaccinate with 1 or more doses.
Influenza	Annual immunization with the current vaccine is recommended regardless of age.
elPV (enhanced-potency inactivated polio vaccine)	In adults ≥ 18 years, use only if specifically indicated: travel to developing countries (probably not Central or South America), prior to (~8 weeks, time for initial 2 doses) household exposure to individuals given oral polio vaccine.
OPV (oral polio vaccine)	Contraindicated
Specific immunoglobulins: Hepatitis B (HBIG), human rabies (HRIG), tetanus (TIG), vaccinia (VIG), varicella-zoster (VZIG)	Can be used for same indications, same dosage as in non-HIV infected individuals

* For further details, see Wilson, et al., Ann Int Med 114:582, 1991

TABLE 14A

MEASURES TO BE TAKEN BY PHYSICIANS IN PREPARING HIV+ PATIENTS AND INDIVIDUALS LIKELY TO HAVE "RISKY" BEHAVIOR FOR OVERSEAS TRAVEL*

The likelihood of developing an illness during a 3-week vacation in a tropical area is about 50%. Since illnesses are likely to be more serious and/or become chronic in the HIV+ patient, there is advice to be given and measures to be taken to minimize risks. These include:

- If the traveler is likely to engage in risky behavior during travel, ascertain the HIV antibody status before travel, especially if travel is planned to a developing country.
- If the traveler is known to be HIV+, take account of legal restrictions on travel for persons with HIV infection[†]. Assess the immune status (CD4 cell count) in infected persons.
- Review planned itinerary and activities in light of the patient's immune status and review the added risks for travel, especially to developing or tropical countries. In some instances, it may be prudent to recommend a change in itinerary or activities because of serious risks that cannot be eliminated or reduced.

- Recommend the following measures to reduce exposure to pathogens:
Assiduously avoid food and beverages that may be contaminated, especially raw or undercooked shellfish, fish, meat, or eggs; raw, unpeeled fruits and vegetables; tap water and ice; as well as unpasteurized milk and milk products (cheese). Insist on eating only well-cooked foods and on drinking only very hot or bottled beverages.
Reduce contact with vectors, for example, by using insect repellent and avoiding outdoor exposure at dusk or other times and places of increased insect activity.
- Urge the patient to obtain prompt evaluation of symptoms of illness and early treatment of infection. Where possible, identify a physician knowledgeable about HIV infection at the destination¹. Arrange for continuation of medical management during travel (for example, prophylaxis for *Pneumocystis carinii* pneumonia).
- Use vaccine and prophylactic therapy as indicated by the planned itinerary and activities. Prescribe antimicrobial agents (with or without antimotility drugs) and counsel the patient on their use for early treatment of diarrheal disease.⁴

¹ The most up-to-date source is: Health Information for the International Traveler, 1993. HHS Publication (CDC) No. 93-8280. Available from U.S. Government Printing Office, Washington, DC 20402.

² Duckett M., Orkin AJ: AIDS-related migration and travel policies and restrictions: a global survey. *AIDS* 3:(Suppl 1) S231-252, 1989.

³ For a list of English-speaking doctors abroad and health information: International Association for Medical Assistance to Travelers (IAMAT), 417 Center St., Lewiston, NY 14092.

⁴ For suggestions regarding a medical kit and advice (for all travelers): Sanford JP: Self-help for the traveler who becomes ill. *Int Dis Clin NA* 6:405, 1992.

* Reproduced with permission from Wilson ME, von Reyn CF, Fineberg HV: Infections in HIV-infected travelers: risks and prevention (Table 2). *Ann Int Med* 114:582, 1991

TABLE 14B
IMMUNIZATION OF HIV+ ADULTS TRAVELING TO DEVELOPING COUNTRIES*

VACCINE/TOXOID/ AGENT	HIV STATUS**		COMMENTS
	ASYMPTOMATIC	SYMPTOMATIC	
"Routine" for All Developing Countries			
eIPV	Yes	Yes	See above. OPV contraindicated
Typhoid (inactivated)	Yes	Yes	Boosters recommended q3 yrs. Live attenuated typhoid vaccine contraindicated
Immune globulin (IG)	Yes	Yes	For 2-3 months travel, 0.02 ml/kg IM single dose
"Special" Depending on Itinerary: Country and Activity			
Cholera (inactivated vaccine)	See Comments	See Comments	Vaccine does not prevent transmission, efficacy ~ 50%, risk to U.S. travelers very low. WHO does not recommend, but some countries require (check with Health Dept.). If required, have vaccination completed, signed, dated and validated to avoid risk of revaccination and quarantine.
Rabies (pre-exposure) (inactivated vaccine)	Yes, if indicated (Animal handlers, travelers spending 1 month or more in country where rabies is a constant threat)	Yes, if indicated	Course: Three 1.0 ml of HDCV or RVA IM on days 0, 7, 28. Test serum for antibodies 2 weeks after 3rd dose.
Meningococcal (polysaccharide vaccine)	Yes, if traveling to area where meningococcal disease is epidemic or endemic (sub Sahara Africa)		
Yellow Fever (live attenuated)	Yes (±); offer choice if potential exposure unavoidable	No (contraindicated)	
Japanese Encephalitis	Yes, if indicated: travel to Asia, especially in monsoon (summer) months, staying in rural areas		Requires 3 injections: day 0, 7, and 30. An abbreviated schedule at days 0, 7, 14 can be used but less effective (MMWR 42:RR-1, 1993).
Plague (inactivated)	Yes, if indicated: to areas of endemic plague, especially if staying in rural areas, not in tourist hotels		
BCG (Bacillus Calmette-Guerin) vaccine	No	No	Is live attenuated vaccine

* All travelers should have current routine immunizations, Table 13, pages 91-92

** Asymptomatic—CDC category A1, A2/Walter Reed Stages 1-4; Symptomatic—CDC A3, B1-3, C1-3/WR Stages 5-6 (see Table 3, pages 10-11).

TABLE 15
PHARMACOKINETICS OF ANTIRETROVIRAL DRUGS AND DRUGS USED IN TREATMENT OF
HIV-ASSOCIATED INFECTIONS IN ADULTS

DRUG	ORAL ABSORPTION (%)	SERUM HALF-LIFE (t/2)(hr)	PEAK SERUM LEVELS ¹ (µg/ml)	PROTEIN BINDING (%)	AVG. CSF PENETRATION (%)	RENAL EXCRETION (%)
Antiretroviral Agents:²						
Zidovudine	42-95	0.6-1.7	1.2 ³	35	15-20	63-95 ⁴
Didanosine (ddI)	37 ⁵	1.5	0.6-2.9 ⁶	< 5	19-21	20
Zalcitabine (ddC)	> 80	1.2-1.8	4-11 ng/ml ⁶	2	20	62-75
Stavudine (d4T)	85	1.1	1.2	"not"	9	40
Lamivudine (3TC)		6.3	3.3			
Antiparasitic Agents:						
Atovaquone	4x ↑ with fatty food	2.2 days	9.6	> 99.9	< 1	< 1
Clindamycin	75	2.4	7.7	85-94	None	10-15
Dapsone	86-100	28	2.3	70-90	+	70-85 ⁴
Iodoquinol	< 10	NA	NA	NA	0	0
Metronidazole	90	6-14	20-25 (IV)	20	16-43	< 20
Pentamidine IV	None	9.4	0.6 (IV)	69	None	80
Primaquine	96	7	0.2			< 5
Pyrimethamine	+	95-118	0.13-0.4	87	13-26	Low
Sulfadiazine	Good	17	100-150 (IV)	45	High	Most
Trimethoprim	Good	11	2.0	44	30 (I)	50-80
TMP/SMX	Good	10/11	1/40 (O) 9/106 (IV)	44/70	50/40	67/84
Trimetrexate	None	11		95		10-30
Antifungal Agents:						
Amphotericin B	None	24	0.5-2.0	> 90	< 2.5	40
Fluconazole	85	20-30	4-8	11	80	65
Flucytosine	78-89	2.4-4.8	70-80	3-4	High	90
Ketoconazole	75 ⁵	8	3.5	99	< 10	2
Itraconazole	55-99	20-30	0.1-0.3	99	< 10	1-18
Miconazole	50	24	7.5-10	90	< 10	< 5
Antiviral Agents:						
Acyclovir	15-30	2.5	0.5-1.0 (O)	9-33	50 (I)	15
Foscarnet	None	0.5-6	445-579 µM/L	14-17	43	80-82
Ganciclovir	< 7	2.9	9.5 ⁶	1-2	25-70	90
Antimycobacterial Agents:						
Isoniazid	90	1	1-5	Low	90	50-70
Rifampin	90-95	2-3	7	80	10-20	3-30
Ethambutol	77	3-4	2-4	40	50 (I)	> 50
Ethionamide	80	3	20	30	~ 100	1-5
Pyrazinamide	Good	9-10	30-50		> 90	70
Cycloserine	Good	10	25-30	< 20	50-80	60-70
Streptomycin	None	3	20-30	Low	±	60-90
Amikacin	None	2	21	0-11	10-24	98
Capreomycin	None	4-6	30 (IM)			57
Clofazimine	45-62	8 days	0.7-1.0		None	< 1
Ciprofloxacin	70	4	4.3	20-40	5-19	40-50
Ofloxacin	98	7	3.5-5.3	32	8-20	70-80
Azithromycin	37	40	0.4	12-50	< 1	5
Clarithromycin	50	5-7	2-3	65-70		30
Rifabutin	53	45	0.2-1.0	85		50 ⁴

Abbreviations: µM = micromolar, NA = not applicable, (IV) = after IV dosing, (IM) = after IM dosing, (I) = inflamed meninges, (O) = after oral dosing

¹ Levels following "usual dose", Tables 6A, 9; ² Intracellular half-life may be more important; ³ In children 2-89%; chewable tablets absorption ↑ 20-25%; ⁴ > 75% excreted as inactive metabolites; ⁵ Requires gastric acid for absorption; ⁶ ZDV 1 µg/ml = 3.74 µM/L, ddI 1 µg/ml = 5.0 µM/L; ddC 1 ng/ml = 4.76 nmol/L, ganciclovir 1 µg/ml = 3.92 µM/L

- I. Immediate Measures (optimally should be done by exposed individual before seeking medical consultation):
Decontaminate:
Skin: Wash thoroughly with soap and water
Eye: Rinse thoroughly with sterile saline, eye irrigant, clean water flush (analogous to chemical splash to the eye)
Mouth, nose: Clean water rinse/flush
- II. Evaluation of Exposure Severity (should be done by an individual trained/experienced in such evaluations; evaluation should be thorough and standardized, information including the immediate measures taken should be documented. ALL RECORDS MUST BE CONFIDENTIAL!):
A. Nature of exposure
Needlestick: Site of injury (draw location)
Gauge of needle if known (if not, estimate)
Needle device in use
Mechanism of occurrence (i.e., recapping a needle)
Depth of needlestick
Visible bleeding at needlestick site
Volume injected, if any
Laceration/cut: Site of injury
Instrument involved (i.e., scalpel blade, test tube)
Mechanism of occurrence
Depth of laceration or cut
Mucosal Splash: Site of splash, volume and duration of contact
Volume (estimate)
Non-intact skin (i.e., eczema, previous burn, blister, scratch):
Site of exposure and mechanism of occurrence
Nature of underlying skin injury/disease
[NOTE: Average needlestick transmission risk is 0.2–0.3%, but individual risk may be higher (if large volume exposure or source with high level viremia, i.e., seroconversion or late stage disease) or lower (if needlestick is superficial and source is asymptomatic)]. Best estimate of mucosal transmission is $\leq 0.9\%$ (*Arch Int Med* 153:1451, 1993).
B. Source fluid/secretion
Fluids with known risk of HIV transmission: blood, bloody body fluids, semen, vaginal fluids, concentrated HIV materials in research labs
Fluids with suspected risk of HIV transmission: pleural fluid, cerebrospinal fluid, peritoneal fluid, synovial fluid, pericardial fluid, amniotic fluid
Materials with doubtful risk of HIV transmission: feces, vomitus, urine, saliva, sweat, tears (unless bloody)
C. Source individual (record name; if patient, record number)
Known HIV positive: record stage of illness, CD4 count (if known), antiretroviral rx history
HIV risk behaviors (male homosexual/bisexual, injection drug use, multiple sex partners (male or female), multiple transfusions before 1985, hemophiliac): request consent to test (HIV and hepatitis B)
HIV risk factors not present: testing is low yield, especially in low prevalence areas
- III. Post-Exposure Care:
A. Counseling: Address anxiety (recognize stress syndromes), where appropriate discuss safer sex/third party risks, HIV pre- and post-test counseling
B. HIV testing:
Baseline serum is essential to document occurrence of infection. If HIV testing is refused, bank serum for later testing if indicated. Obtain specimen before HBIG is given if HBIG is required since HBsAg testing is usually performed.
Follow-up: repeat HIV tests at 6 weeks, 3 months, and 6 months. If negative at 6 months, assume HIV infection did not occur (because seroconversion window is rarely more than 6 months; assurance cannot be absolute, but nearly so). All reported HCW seroconversions have occurred before 6 months, even with ZDV rx.
C. Chemoprophylaxis: **Administration of zidovudine for post-exposure prophylaxis is experimental.** Data from animal and human studies are inadequate to establish the efficacy (if any) for prophylaxis after occupational exposure. At least 8 treatment failures have been documented. Current recommendations at San Francisco General Hospital are based on exposure level:
Massive: e.g., transfusion—recommended
Definite parenteral: e.g., intramuscular injection of blood, large-bore hollow needle—endorsed
Possible parenteral: e.g., subcutaneous, superficial punctures, mucosal contacts (especially if source pt has seroconversion illness or advanced disease)—available
Doubtful parenteral: e.g., non-bloody fluid—discouraged
Non-parenteral: e.g., cutaneous—not provided

The Collaborative Chemoprophylaxis Study Group Protocol is: Zidovudine 200 mg po q4h x 72 hrs (start as soon as possible, ideally within 1 hour of exposure) then 100-200 mg q4h (5x/day) for 25 days. Hematologic monitoring is indicated during rx.

Treatment is deferred for women who are pregnant or breast feeding and for men and women who decline contraception during the follow-up period (6 months). To date, objective toxicity has not been observed but intolerance (GI, fatigue, headache) is common. Treatment usually not provided if > 72 hours post-exposure. If source pt has been on ZDV for ≥ 6 months, some have recommended ZDV as above + ddI 200 mg po immediately, then 200 mg po q12h, duration ?, probably 25 days (*Lancet* 341:112, 1993).

D. Seroconversion: The acute HIV conversion syndrome (fever, rash (usually morbilliform), pharyngitis, lymphadenopathy (an infectious mononucleosis syndrome)) is common in the subset of health care workers who become infected. If such occurs, obtain serum for ELISA, Western blot and p24 antigen.

TABLE 17
TREATMENT OF HIV/AIDS-ASSOCIATED MALIGNANCIES *

DISEASE	DRUGS/MODALITIES/REGIMENS	COMMENTS
Kaposi's Sarcoma (KS) Indications: • Painful or bulky lesion, especially oral/pharyngeal • Lymphedema • Pulmonary KS • Rapidly progressive disease	Local (treatment is palliative only)	
	Radiotherapy: Single 800 cGy or equal fractionated dose	Highly effective for local palliation
	Laser surgery	Effective vs intraoral lesions
	Intralesional chemotherapy: 0.1 ml vinblastine (0.1–0.5 mg/ml in 1% bicarbonate-buffered lidocaine) (<i>Am Acad Derm</i> 28:61, 1993) (using tuberculin syringe)	For cosmetic purposes. Repeated rx may be necessary. Hyperpigmented area may remain after rx.
	Cryotherapy with liquid nitrogen	For isolated small lesions
For more rapidly progressive or advanced widespread symptomatic disease	Systemic (chemotherapy is palliative only, does not alter survival)	
	Vincristine (Oncovin) 1.5–2.0 mg/week IV (mix only in normal saline or glucose in water)	Response: 20–60%. Toxicity: neuromuscular—sensory loss, paresthesia, difficulty in walking
	Vinblastine (Velban) 0.05–0.1 mg/kg/week IV (do not give next dose until WBC > 4000/mm ³)	Response: 25–30%. Toxicity: myelosuppression, especially leucopenia
	Etoposide (VP16) (VePesid) 50–100 mg/M ² IV qd for 3 days every 3–4 weeks or 50 mg po qd for 2–3 weeks, depending on neutrophil count	Response: 75%. Toxicity: leucopenia, thrombocytopenia, GI, alopecia
	Doxorubicin (Adriamycin, Rubex) 20 mg/M ² IV every other week	Response: 53%. Toxicity: myelosuppression. As total dose approaches 550 mg/M ² serious myocardial toxicity with uncontrollable heart failure
	Bleomycin (Blenoxane) 10–15 units/M ² IV, IM or SC every 14 days (used with vincristine for patients with myelosuppression)	Toxicity: anaphylactoid reactions (fever, chills, hypotension, wheezing) (1%) with initial doses. Pulmonary fibrosis (10% of older patients after ≥ 400 units) but may occur with lesser doses and in younger patients. Non-myelosuppressive
	Vincristine-vinblastine combination: alternate weeks of vincristine 2 mg/week and vinblastine 0.1 mg/kg/week IV	Response: 45%
	Vincristine-bleomycin combination: vincristine 2 mg IV + bleomycin 10 units/M ² IV every 14 days	Response: for pulmonary KS 100%. Non-myelosuppressive
	Doxorubicin-bleomycin-vincristine combination: doxorubicin 10–20 mg/M ² + bleomycin 10 units/M ² + vincristine 1.5–2.0 mg IV every 14 days	Response: 87%. Most active combination. Useful for advanced symptomatic disease. Rapid response possible.
Non-Hodgkin's Lymphoma	Interferon alfa-zidovudine combination: interferon alfa 4–18 million units/day SC + zidovudine 600 mg qd (divided into 3 doses) po	Poor response if CD4 < 100/mm ³ . Occurs slowly. Toxicity: Interferon: flu-like symptoms > 90% (fatigue, fever, myalgia, headache, arthralgia), GI (anorexia, nausea, diarrhea). Zidovudine: leucopenia 2%, anemia 1%
	Multi-agent chemotherapeutic regimens have had moderate impact on survival but less than in non-HIV+ patients with non-Hodgkin's lymphomas. Less aggressive regimens appear to be better tolerated and thus give better outcome in many patients. Survival directly related to CD4 count. If CD4 < 100, results are so poor that many would not recommend rx.	

or drugs, review package insert regarding dosage, precautions in administration and toxicities. For details, see Kaplan LD: Malignancies associated with AIDS. In *Medical Management of AIDS*, 4th Ed., Ed.: Sande MA, Volberding PA, W.B. Saunders, Philadelphia, 1994

DISEASE	DRUGS/MODALITIES/REGIMENS	COMMENTS
Non-Hodgkin's Lymphoma (continued)	A modified m-BACOD regimen: Day 1: Cyclophosphamide 300 mg/M² IV Doxorubicin 25 mg/M² IV Vincristine 1.4 mg/M² IV (not to exceed 2.0 mg) Bleomycin 4 units/M² IV Dexamethasone 3 mg/M² po (days 1-5) Day 15: Methotrexate (MTX) 500 mg/M² with leucovorin rescue 25 mg po q6h x 4 beginning 6 hours after completion of MTX CNS: Cytosine arabinoside 50 mg intrathecally on days 1, 8, 21, 28. Add Helmet-Field irradiation if marrow (+) 2000 cGy or if CSF (+) 4000 cGy. Rx: 4-6 cycles at 28-day intervals. Start zidovudine 200 mg q4h at completion of chemotherapy	Response: complete remission rate ~50% (of 42 patients). Only 4 patients with complete remission relapsed (14 months). With CNS rx, no isolated CNS relapse (<i>Blood</i> 74:897a, 1989; <i>Rev Inf Dis</i> 12:938, 1990; <i>JAMA</i> 266:84, 1991). Only 10% of cycles complicated by neutropenia of < 500/mm³. Median survival 6.5 months.
Primary CNS Lymphoma	Whole brain radiotherapy; 4000 cGy	Response: clinical improvement 76%, radiographic improvement 69%. Median survival 2-5 months.
Cervical Carcinoma (85-90% squamous cell)	Radiotherapy and surgery used alone or together	Cure rates nearly identical
Rectal Carcinoma (majority are epidermoid)	Wide surgical resection. When not curative limited palliative surgery may be indicated. Only drug with proven efficacy is 5-fluorouracil.	Relative risk is 84x ↑ in homosexual men with AIDS (<i>Lancet</i> 343:636, 1994). ↑ serum carcinoembryonic antigen (CEA) is not specific, but ↑ in 70% of patients with colorectal carcinoma

TABLE 18
DRUG DOSAGE ADJUSTMENTS IN
RENAL AND/OR HEPATIC DYSFUNCTION

(The data below are largely, but not entirely, an adaptation from Bennett et al., *DRUG PRESCRIBING IN RENAL FAILURE*, 3rd Ed., American College of Physicians, 1994.)

Excretion of native drugs and/or their metabolites is via the kidney or biliary tract; hence, renal or hepatic disease can result in toxic serum concentrations. This table provides general guidance with several qualifications. For many drugs, there is incomplete knowledge of the influence of impaired organ function on drug excretion; much more is known about the influence of renal failure as compared to hepatic failure. The role of metabolites is often unknown.

The information presented emphasizes drugs often employed to treat HIV or an opportunistic infection in an AIDS patient. Similar guidance for other antimicrobial drugs can be found in Table 21 of the 1994 *SANFORD GUIDE TO ANTIMICROBIAL THERAPY*.

The following drug adjustments are based on the patient's estimated endogenous creatinine clearance, which can be calculated as:

$$\frac{(140 - \text{age}) (\text{ideal body weight in kg})}{(72) (\text{serum creatinine, mg/dl})} \text{ for men} \quad (0.85 \text{ for females})^*$$

Ideal body weight for men: 50.0 kg + 2.3 kg per inch over 5 feet

Ideal body weight for women: 45.5 kg + 2.3 kg per inch over 5 feet

* The estimated creatinine clearance is used as a measure of glomerular filtration rate

In this table, virtually all dosage adjustments are calculated by extending the interval between doses rather than decreasing the size of each individual dose. The interval method provides the greatest patient comfort, lends itself to outpatient administration, and is most cost-effective. For selected infections, data may emerge indicating superiority of a dose reduction method; guidance for the latter is available in the above reference.

The table indicates those drugs sufficiently cleared by dialysis that a supplemental dose after dialysis is recommended. The table suggests dosage adjustments for patients that require hemodialysis (Hemo), chronic ambulatory peritoneal dialysis (CAPD), and continuous arteriovenous hemofiltration (CAVH).

Unfortunately, to date there is no recognized method of correlating a laboratory indicator of severity of liver disease to a magnitude of reduction of drug dosage. The clinician estimates, and then, when possible, the appropriateness of the new dosage is validated by serum level measurements.

TABLE 18 (2)

DRUG DOSAGE ADJUSTMENTS IN RENAL/HEPATIC DYSFUNCTION

DRUG	DOSE FOR ESTIMATED CrCl >90 ml/min	ADJUSTMENT FOR RENAL FAILURE BY GFR, ml/min			SUPPLEMENT FOR DIALYSIS: HEMO, CAPD, CAVH	DOSE REDUCTION FOR HEPATIC DYSFUNCTION (Liver Chemistries 4-5x > Normal)
		> 50-90	10-50	< 10		
Antibacterial						
<u>Aminoglycosides</u> (traditional)						
Amikacin	7.5 mg/kg q12h	q12h	q12-18h	q24-48h	Hemo: 5-7 mg/kg after dialysis CAPD: 6-12 mg/L/ea exchange CAVH: as for GFR 10-50 & check levels	No
Streptomycin	7.5 mg/kg q12h	q12h	q12-18h	q24-48h		No
<u>Aminoglycosides</u> (once-daily dosing)						
Amikacin	15 mg/kg q24h	7.5-15 mg/kg q24h	4.0-7.5 mg/kg q24-48h	3.0 mg/kg q48h	Hemo: 5-7 mg/kg after dialysis CAPD: 60 mg/L in one exchange per day only CAVH: as for GFR 10-50	
Streptomycin	15 mg/kg q24h	7.5-15 mg/kg q24h	4.0-7.5 mg/kg q24-48h	3.0 mg/kg q48h		
<u>Cephalosporins/Penicillins/Beta-Lactamase Inhibitors/Carbapenem</u> : See Table 21, Sanford GUIDE TO ANTIMICROBIAL THERAPY, 1994						
<u>Fluoroquinolones</u>						
Ciprofloxacin	250-750 mg po q12h 400 mg IV q12h	q12h q12h	q12-24h q12-24h	q24h q24h	Hemo: 250 mg po q12h CAPD: 250 mg po q8h CAVH: 200 mg IV q12h	Yes
Ofloxacin	200-400 mg po or IV bid	q12h	q24h	q48h	Hemo: 100 mg po, IV bid CAPD: 200-400 mg q48h CAVH: 300 mg qd	Yes
<u>Macrolides</u>						
Azithromycin	500 mg x1, then 250 mg q24h	q24h	q24h	q24h	Hemo: None CAPD: None CAVH: None	Yes
Clarithromycin	0.5-1.0 gm q12h	q12h	q12-24h	q24h	Hemo: Dose post-dialysis CAPD: None CAVH: None	Yes
Erythromycin	250-500 mg q6h	q6h	q6h	q8-12h	Hemo: None CAPD: None CAVH: None	Yes
<u>Tetracyclines</u>						
Doxycycline	100 mg q12h	q12h	q12h	q12h	Hemo: None CAPD: None CAVH: None	Yes

TABLE 18 (3)

DRUG	DOSE FOR ESTIMATED CrCl >90 ml/min	ADJUSTMENT FOR RENAL FAILURE BY GFR, ml/min			SUPPLEMENT FOR DIALYSIS: HEMO, CAPD, CAVH	DOSE REDUCTION FOR HEPATIC DYSFUNCTION (Liver Chemistries 4-5x > Normal)
		> 50-90	10-50	< 10		
Tetracycline	250-500 mg q6h	q8-12h	q12-24h	q24h	Hemo: None CAPD: None CAVH: None	Yes
Miscellaneous						
Clindamycin	150-450 mg po q6h	q6h	q6h	q6h	Hemo: None CAPD: None CAVH: None	Yes
Metronidazole	7.5 mg/kg q6h	q6h	q6h	q12h	Hemo: Dose after dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR 10-50	Yes
Sulfadiazine	0.5-1.0 gm q6h	q12h	q24h	Avoid	Hemo: No data CAPD: No data CAVH: Dose for GFR 10-50	No
Sulfamethoxazole	1.0 gm q6h	q12h	q12-24h	q24h	Hemo: 1 gm after dialysis CAPD: 1 gm q24h CAVH: Dose for GFR 10-50	No
Trimethoprim	100-200 mg q12h	q12h	q12-24h	q24h	Hemo: Dose after dialysis CAPD: q24h CAVH: Dose for GFR 10-50	No
Antifungal Antibiotics						
Amphotericin B	0.4-1.0 mg/kg q24h	q24h	q24h	q24-48h	Hemo: None CAPD: Dose for GFR <10 CAVH: Dose for GFR 10-50	No
Fluconazole	100-400 mg q24h	q24h	q24-48h	q48-72h	Hemo: 200 mg post-dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR 10-50	Yes
Flucytosine	37.5 mg/kg q6h (Dose-dependent marrow suppression. Goal is therapeutic level of 20 µg/ml)	q12h	q12-24h	q24h	Hemo: Dose after dialysis CAPD: 0.5-1.0 gm q24h CAVH: Dose for GFR 10-50	No
Itraconazole	100-200 mg q12h	q12h	q12h	q12-24h	Hemo: 100 mg q12-24h CAPD: 100 mg q12-24h CAVH: 100 mg q12-24h	Yes

TABLE 18 (4)

DRUG	DOSE FOR ESTIMATED CrCl > 90 ml/min	ADJUSTMENT FOR RENAL FAILURE BY GFR, ml/min			SUPPLEMENT FOR DIALYSIS: HEMO, CAPD, CAVH	DOSE REDUCTION FOR HEPATIC DYSFUNCTION (Liver Chemistries 4-5x > Normal)	
		> 50-90	10-50	< 10			
Ketoconazole	200 mg q24h	q24h	q24h	q24h	Hemo: None CAPD: None CAVH: None	Yes	
Antiparasitic/Antiprotozoan Drugs							
Atovaquone	750 mg q8h	Pharmacokinetics have not been studied in patients with renal or hepatic impairment					No
Dapsone	100 mg q24h	Renal excretion, but data inadequate for guidance. Advise dosage reduction with renal impairment					
Paromomycin	Not absorbed. No adjustment necessary						
Pentamidine	4 mg/kg q24h	q24h	q24-36h	q48h	Hemo: None CAPD: None CAVH: None	No	
Primaquine	15 mg base q24h	Data insufficient for guidance					Theoretic risk of metabolite accumulation
Pyrimethamine	50-75 mg q24h (Doses for treatment of toxoplasmosis. Antimalarial doses much lower)	q24h	q24h	q24h	Hemo: None CAPD: None CAVH: None		
Antituberculous Drugs (see aminoglycosides, macrolides and quinolones above)							
Clofazimine	100 mg q24h	q24h	q24h	q24h	No dialysis data	Yes	
Ethambutol	15 mg/kg q24h	q24h	q36h	q48h	Hemo: Dose after dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR 10-50	No data	
Isoniazid	5 mg/kg q24h (Max of 300 mg/day)	q24h	q24h	q24h	Hemo: Dose after dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR <10	Yes	
Pyrazinamide	25 mg/kg q24h	q24h	q48-72h	q72h	Hemo: 12 mg/kg dose CAPD: No data CAVH: Avoid	No data	
Rifabutin	300 mg q24h	No data available			Hemo: None CAPD: Dose for GFR <10 CAVH: Dose for GFR <10	Yes	
Rifampin	600 mg q24h	q24h	q24-48h	q48h			

TABLE 18 (5)

DRUG	DOSE FOR ESTIMATED CrCl >90 ml/min	ADJUSTMENT FOR RENAL FAILURE BY GFR, ml/min			SUPPLEMENT FOR DIALYSIS: HEMO, CAPD, CAVH	DOSE REDUCTION FOR HEPATIC DYSFUNCTION (Liver Chemistries 4-5x > Normal)
		> 50-90	10-50	< 10		
Antiviral Drugs						
Acyclovir	5-12.4 mg/kg q8h	q8h	q12-24h	q24-48h	Hemo: Dose after dialysis CAPD: Dose for GFR <10 CAVH: 3.5 mg/kg/day	No
Didanosine (ddI)	125-200 mg q12h	q12h	q24h	q48h	Hemo: Dose post-dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR <10	No data
Foscarnet Induction Maintenance	50-60 mg/kg q8h 90-120 mg/kg q24h (NOTE: Doses estimates only—data incomplete)	q18h	q24h	q72h	Hemo: 50 mg/kg dose post-dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR 10–50	No data
Ganciclovir	5 mg/kg q12h	q12-24h	q24-48h	q48-96h	Hemo: Dose after dialysis CAPD: Dose for GFR <10 CAVH: 2.5 mg/kg/day	No data
Interferon alfa	3-36 mIU q24h	No data for guidance				
Zalcitabine (ddC)	0.375-0.75 mg q8h	q8h	q12h	q24h	No dialysis data	No data
Zidovudine (ZDV)	200 mg q8h	q8h	q8h	q12-24h	Hemo: 100 mg after dialysis CAPD: Dose for GFR <10 CAVH: Dose for GFR 10–50	No data

TABLE 19

DRUG/DRUG INTERACTIONS: ANTIRETROVIRAL DRUGS and DRUGS USED IN TREATMENT OF HIV-ASSOCIATED INFECTIONS AND MALIGNANCIES

DRUG A	DRUG B	EFFECT	SIGNIFICANCE
ANTIRETROVIRAL DRUGS			
Didanosine (ddI)	Dapsone	↓ absorption of dapsone (requires gastric acid for absorption, buffer in ddI neutralizes) (give 2 hrs before or after ddI)	+
	Ketoconazole	↓ absorption of ketoconazole (requires gastric acid for absorption, ddI buffer neutralizes) (administer 2 hrs before or after ddI)	+
	Itraconazole	↓ absorption of Itra (give 2 hrs before or after ddI)	±
	Fluoroquinolones (ciprofloxacin, ofloxacin), Tetracyclines	↓ absorption of fluoroquinolones and tetracyclines (buffer in ddI contains Mg, Al which bind the FQ, tetracycline). Take antibiotics at least 2 hours before ddI.	+
	Drugs associated with pancreatitis	Alcohol, asparaginase, azathioprine, estrogens, furosemide, methylodopa, nitrofurantoin, pentamidine (IV), sulindac, thiazide diuretics, valproic acid may ↑ risk of pancreatitis	±
	Drugs associated with peripheral neuropathy	Cisplatin, dapsone, ethambutol, ethionamide, isoniazid, lithium, metronidazole, nitrofurantoin, nitrous oxide, phenytoin, vincristine, zalcitabine may ↑ risk of neuropathy	±
	Drugs (other) whose absorption is decreased by antacids	Digoxin, propranolol/atenolol, ranitidine/cimetidine, INH, metronidazole	+
Zidovudine (ZDV)	Acetaminophen	↓ ZDV blood levels (acetaminophen ↑ clearance of ZDV). If rx > 1 week, use ibuprofen or naproxen	±
	Amphotericin B	↑ hematotoxicity of ZDV (ampho B ↓ renal clearance of ZDV)	+
	Flucytosine	↑ hematotoxicity of ZDV (flucytosine ↓ renal clearance of ZDV)	+
	Fluconazole	↑ ZDV blood levels	±
	Ganciclovir	↑ hematotoxicity (neutropenia)	+
	Indomethacin	↓ ZDV blood levels (indomethacin ↑ clearance of ZDV)	±
	Interferon alfa, beta	↑ ZDV toxicity	±
	Pentamidine	↑ ZDV toxicity	±
	Phenytoin	↓ or ↑ phenytoin levels (usually ↓ levels)	+
	Probenecid	↑ levels of ZDV, ↑ frequency of rash	+
	Pyrimethamine	↓ antitoxoplasma activity of pyrimethamine; ↓ ZDV clearance	+
	Ribavirin	↓ levels of ZDV	±
	Rilampin	↓ ZDV levels	±
	Valproic acid	↑ levels of ZDV	±
	Drugs associated with hematotoxicity	Dapsone, pentamidine, TMP/SMX, vincristine, vinblastine, doxorubicin, interferon may ↑ hematotoxicity	±
Zalcitabine (ddC)	Drugs associated with peripheral neuropathy	Cisplatin, dapsone, ethambutol, ethionamide, isoniazid, lithium, metronidazole, nitrofurantoin, nitrous oxide, phenytoin, vincristine may ↑ risk of neuropathy	±
	Foscarnet	↑ toxicity of ddC	+
	Drugs associated with pancreatitis	Valproic acid, pentamidine (IV), alcohol, ddI may ↑ risk of pancreatitis	+
ANTIPARASITIC DRUGS			
Atovaquone	Has not been studied, except there is no interaction with phenytoin		
Clindamycin	Kaolin (Donnagel-PG, Kaolin-Pectin Suspension)	↓ absorption of clindamycin	+

TABLE 19 (2)

DRUG A	DRUG B	EFFECT	SIGNIFICANCE
ANTIPARASITIC DRUGS (continued)			
Clindamycin (continued)	Neuromuscular blocking and muscle relaxant agents	↑ frequency and/or prolonged duration of respiratory paralysis. Atracurium, baclofen, cyclobenzaprine, dantrolene, diazepam, methocarbamol	±
	Theophylline	↑ serum levels of theophylline (seizures, apnea)	
Dapsone	Zidovudine	↑ bone marrow toxicity	±
	Chloramphenicol	↑ chloramphenicol blood levels	±
	Cimetidine	↓ formation of metabolite responsible for methemoglobin (= good)	±
	Didanosine	↓ dapsone absorption	+
	Oral contraceptives	Alters GI flora; menstrual changes, ↑ pregnancy	+
	Probenecid	↑ blood levels of dapsone	±
	Pyrimethamine	↑ hematotoxicity	+
	Rifampin	↓ serum half-life of dapsone	±
	Trimethoprim	↑ levels of both dapsone and trimethoprim with ↑ methemoglobinemia	±
Metronidazole	Cyclosporine	↑ cyclosporine levels	?
	Lithium	↑ lithium levels	+
	Phenobarbital	↓ levels of metronidazole	±
	Warfarin (Coumadin)	↑ anticoagulant effect	++
	Barbiturates	↓ levels of metronidazole	+
	Disulfiram (Antabuse)	Acute psychosis or confusion	+
	Ethanol	Acute alcohol intolerance (flushing, nausea, vomiting, tachycardia — disulfiram-like)	+
	Phenytoin	↑ metronidazole levels	±
Paromomycin	Warfarin	↑ prothrombin time (bleeding)	±
Pentamidine-IV	Amphotericin B	4 cases acute renal failure	+
	Foscarnet	Hypocalcemia	+
	Drugs associated with pancreatitis	See listing under <i>ddl</i> . May ↑ risk of pancreatitis	±
Primaquine	Drugs associated with G6PD deficiency hemolysis	Chloroquine, chloramphenicol, dapsone, isoniazid, nalidixic acid, nitroazole, nitrofurantoin, piperazine, probenecid, quinacrine, quinine, sulfonamides, TMP/SMX may ↑ frequency of hemolysis	±
Pyrimethamine	Lorazepam	Mild hepatotoxicity	±
	Sulfonamides, TMP/SMX	↑ risk of bone marrow suppression	±
	Zidovudine	↑ hematotoxicity, ↓ antitoxoplasma activity	±
Sulfadiazine, trimethoprim/sulfamethoxazole (TMP/SMX)	Azathioprine	↑ hematotoxicity	+
	Cyclosporine	↓ cyclosporine levels	+
	Phenytoin	↑ levels of phenytoin (nystagmus, ataxia)	+
	Pyrimethamine	↑ hematotoxicity	+
	Methotrexate	↑ hematotoxicity	+
	Warfarin	↑ prothrombin time (bleeding)	++
	Oral hypoglycemic agents	↑ hypoglycemic effect	+
	Thiopental	↑ thiopental levels	±
ANTIFUNGAL DRUGS			
Amphotericin B	Acyclovir	↑ nephrotoxicity	±
	Aminoglycosides	↑ nephrotoxicity	+
	Cyclosporine	↑ nephrotoxicity	+
	Digitalis	↑ digitalis toxicity (2° to hypokalemia)	+
	Foscarnet	↑ nephrotoxicity	±
	Flucytosine	↑ toxicity of flucytosine 2° to ↑ levels	+
	Zidovudine	↑ hematotoxicity of ZDV	+

DRUG A	DRUG B	EFFECT	SIGNIFICANCE
ANTIFUNGAL DRUGS (continued)			
Fluconazole	Antihistaminics, non-sedating [†]	See footnote 1	
	Carbamazepine	↓ levels of fluconazole	++
	Cimetidine	↓ absorption of fluconazole	+
	Cyclosporine	↑ cyclosporine levels	±
	Contraceptives, oral	↓ levels of contraceptive	?
	Hydrochlorothiazide	↑ levels of fluconazole	+
	Phenytoin	↑ levels of phenytoin (nystagmus, ataxia) ↓ levels of fluconazole	+
	Rifampin	↓ levels of fluconazole (↑ metabolism)	++
	Zidovudine	↑ levels of ZDV	±
	Oral hypoglycemic agents	↑ levels of oral hypoglycemic agents (hypoglycemia). Oral hypoglycemic agents include acetohexamide, chlorpropamide, glibenclamide, glipizide, glyburide, tolbutamide, tolazamide	+
	Warfarin	↑ prothrombin time	+
Flucytosine	Cytosine arabinoside	↓ antifungal activity of flucytosine	±
	Amphotericin B	↑ levels of flucytosine with ↑ hematologic, hepatic toxicity	+
	Ganciclovir	↑ hematotoxicity	
Itraconazole	Antihistaminics, non-sedating [†] (contraindicated)	↑ antihistamine levels, cardiotoxicity	++
	Carbamazepine	↓ levels of itraconazole	++
	Cimetidine and other H ₂ blockers	↓ absorption of itraconazole	+
	Cyclosporine	↑ cyclosporine levels, ↑ nephrotoxicity	+
	Digoxin	↑ digoxin levels	±
	INH	↓ levels of itraconazole	±
	Oral hypoglycemic agents	↑ levels of hypoglycemic agents (hypoglycemia)	+
	Phenytoin	↓ levels of itraconazole	++
	Rifampin	↓ levels of itraconazole	++
	Warfarin	↑ prothrombin time	+
Ketoconazole	Antihistaminics, non-sedating [†] (contraindicated)	↑ cardiotoxicity	++
	Carbamazepine	↓ levels of ketoconazole	++
	Antacids	↓ ketoconazole absorption	++
	H ₂ blockers	↓ ketoconazole absorption	++
	Didanosine	↓ ketoconazole absorption	++
	Benzodiazepines	↑ effect of benzodiazepines	?
	Cyclosporine	↑ nephrotoxicity	+
	Phenytoin	↓ levels of ketoconazole	++
	Rifampin	↑ metabolism of ketoconazole, ↓ absorption of rifampin	++
	Theophylline	↓ levels of theophylline	±
	Warfarin	↑ anticoagulant activity (bleeding)	±
ANTIVIRAL DRUGS			
Acyclovir	Probenecid	↑ acyclovir toxicity	?
	Sulfinpyrazone (Anturane)	May ↑ acyclovir crystalluria	?
	Zidovudine	Marked lethargy reported	?
	Drugs associated with nephrotoxicity	See listing under Foscamet, may ↑ risk of nephrotoxicity and acyclovir toxicity	±

TABLE 19 (4)

DRUG A	DRUG B	EFFECT	SIGNIFI- CANCE
ANTIVIRAL DRUGS (continued)			
Foscarnet	Drugs associated with nephrotoxicity	Acyclovir, aminoglycosides, amphotericin B, cisplatin, cyclosporine may ↑ risk of nephrotoxicity	±
	Clondronate, edetate	Hypocalcemia	+
	Pentamidine-IV	Hypocalcemia (foscarnet complexes with calcium), cardiac toxicity	+
Ganciclovir	Cyclosporine	↑ nephrotoxicity	+
	Imipenem	↑ occurrence of seizures	±
	Probenecid	↑ levels of ganciclovir	+
	Drugs that inhibit renal tubular secretion	Dapsone, pentamidine, flucytosine, vincristine, vinblastine, doxorubicin, amphotericin B, TMP/SMX may ↓ renal clearance of ganciclovir with ↑ toxicity	±
	Drugs associated with hematotoxicity	ZDV, amphotericin B, antineoplastic agents, 5-fluorocytosine	±
ANTIMYCOBACTERIAL DRUGS			
Isoniazid (INH)	Acetaminophen	↓ metabolism of acetaminophen	?
	Aluminum salts	↓ INH absorption (take INH 1 hour before antacid)	+
	Benzodiazepines	↑ effect of benzodiazepine	?
	Carbamazepine	↑ levels of carbamazepine (nausea, vomiting, nystagmus, ataxia)	++
	Corticosteroids	↑ INH metabolism	+
	Cycloserine	↑ CNS toxicity	±
	Phenytoin	↑ phenytoin levels (nystagmus, ataxia)	++
	Disulfiram	Changes in affect	?
	Ketoconazole	↓ absorption of INH, ↑ metabolism of ketoconazole	?
	Oral hypoglycemic agents	↓ hypoglycemic effect	+
	Warfarin	↑ effects of warfarin (bleeding)	±
Rifampin	Azole antifungal agents ²	↓ levels of antifungal agent	+
	Beta adrenergic blockers	↓ effect of β blocker	+
	Clofibrate	↓ effect of clofibrate	±
	Corticosteroids	↑ replacement requirement of corticosteroid	+
	Cyclosporine	↓ effect of cyclosporine	++
	Digitoxin	↓ serum digitoxin levels	±
	Enalapril	↓ effect of enalapril	±
	Ketoconazole	↓ absorption of rifampin, ↑ metabolism of ketoconazole	?
	Methadone	↓ serum levels of methadone (withdrawal)	+
	Mexiletine	↑ levels of mexiletine	?
	Phenytoin	↓ levels of phenytoin	+
	Propafenone	↓ levels of propafenone	±
	Oral contraceptives	↓ effectiveness of contraceptive (spotting, pregnancy)	+
	Quinidine	↓ effect of quinidine	+
	Oral hypoglycemic agents	↓ hypoglycemic effect	±
	Theophylline	↓ theophylline levels	+
	Tocainide (Tonocard)	↓ effect of tocainide	+
	Warfarin	↓ effect of warfarin	++
Ethambutol	Didanosine tablets	↓ ethambutol absorption (tablets buffered with Al salt) (give 2 hrs before or after ddl)	±
	Verapamil	↓ levels of verapamil	±
	Aluminum salts	↓ ethambutol absorption	+

DRUG A	DRUG B	EFFECT	SIGNIFICANCE
ANTIMYCOBACTERIAL DRUGS (continued)			
Ethionamide	"Diabetes mellitus" Antituberculous drugs	Management more difficult, ↑ hepatitis ↑ side effects, convulsions reported, ↑ frequency abnormal liver function tests	±
Pyrazinamide	Drugs associated with hepatotoxicity	Ketoconazole, INH, rifampin may ↑ occurrence of hepatotoxicity	±
Cycloserine	Ethanol	↑ occurrence of seizures (cycloserine contraindicated in active alcoholics)	+
	Isoniazid, ethionamide	↑ CNS effects (drowsiness, dizziness)	+
	Drugs associated with neurotoxicity	See <i>ddl</i> for listing, may ↑ neurologic side effects	±
Amikacin	Amphotericin B	↑ nephrotoxicity	+
	Cephalothin	↑ nephrotoxicity	±
	Cisplatin	↑ nephro- and ototoxicity	±
	Cyclosporine	↑ nephrotoxicity	+
	Loop diuretics	↑ ototoxicity	++
	NSAIDs	↑ nephrotoxicity	+
	Radiographic contrast	↑ nephrotoxicity	+
	Vancomycin	↑ nephrotoxicity	+
Capreomycin	Neuromuscular blocking agents, anesthesia	↑ neuromuscular blockade	+
	Drugs associated with nephrotoxicity	↑ nephro- and ototoxicity	±
Clofazimine	Dapsone	Dapsone may ↓ anti-inflammatory activity of clofazimine	±
Ciprofloxacin	Cimetidine	↑ levels of cip (↓ renal clearance of cip)	+
	Multivalent metallic cations (Al, Ca, Fe, Mg, Zn)	↓ absorption of cip (as much as 90%) (recall Fe, Zn in multivitamin preps) (recall <i>ddl</i> is buffered)	++
	Probenecid	↓ renal clearance of cip	±
	Caffeine	↑ levels of caffeine	+
	H ₂ blockers	↓ absorption of cip	++
	Sucralfate	↓ absorption of cip (~90%)	++
	Metronidazole	Seizures	±
	Opiates	↓ effect of opiates (experimental)	?
	Theophylline	↑ theophylline levels	++
	Warfarin	↑ prothrombin time	+
	Antineoplastic agents	Cyclophosphamide, cytarabine, daunorubicin, doxorubicin, mitoxantrone, prednisolone, vincristine all may ↓ absorption of cip	±

Macrolides (Ery = erythromycin, Azi = azithromycin, Clr = clarithromycin, + = occurs, 0 = does not occur, NR/NS = not reported but not studied):

Ery	Azi	Clr			
+	NR,NS	NR,NS	Allentaniil	↑ action of B	±
+	NR,NS	+	Carbamazepine	↑ serum levels of B, nystagmus, nausea, vomiting, ataxia	++ (avoid with erythro)
+	NR,NS	NR,NS	Corticosteroids	↑ effects of B	+
+	NR,NS	NR,NS	Cyclosporine	↑ serum levels of B	+
+	NR,NS	NR,NS	Digoxin	↑ serum levels of B (10% of cases)	+
+	NR,NS	NR,NS	Felodipine	↑ levels of B	±
+	NR,NS	NR,NS	Lovastatin	Rhabdomyolysis	±
+	NR,NS	NR,NS	Ergot alkaloids	Peripheral ischemia	±

See page 108 for footnotes

DRUG A			DRUG B	EFFECT	SIGNIFI- CANCE
Macrolides (continued)					
Ery	Azi	Clr			
+	0	+	Antihistaminics, non-sedating ¹	↑ cardiotoxicity	+
+	0	+	Theophylline	↑ serum levels of B: nausea, vomiting, seizures, apnea	++
+	0	NR,NS	Oral anticoagulants	May ↑ prothrombin time	?
+	NR,NS	NR,NS	Valproic acid	↑ levels of B	±
NR,NS	0	+	Zidovudine	↓ levels of B	±
ANTINEOPLASTIC DRUGS					
Bleomycin			Digoxin	↓ digoxin levels	±
			Phenytoin	↓ phenytoin levels	±
Doxorubicin			Fluoroquinolones	↓ absorption of fluoroquinolones	+
			Digoxin	↓ digoxin levels	±
			Barbiturates	↑ plasma clearance of doxorubicin	±
			Phenytoin	↓ phenytoin levels	+
			Zidovudine	↑ hematotoxicity	±
Etoposide (VP16)			Warfarin	↑ anticoagulant effect	±
Vinblastine			Interferon alfa	↑ interferon toxicity	±
			Phenytoin	↓ levels of phenytoin	+
			Zidovudine	↑ hematotoxicity	±
Vincristine			Digoxin	↓ digoxin levels	±
			Fluoroquinolones	↓ absorption of fluoroquinolones	±
			Nifedipine	↓ clearance of vincristine	+
			Zidovudine	↑ hematotoxicity	±
			Zalcitabine	May have ↑ risk of neuropathy	±
			Didanosine	May have ↑ risk of neuropathy	±

¹ Antihistaminics, non-sedating: astemizole, loratadine, terfenadine. Interaction reported with ketoconazole, itraconazole, not with fluconazole. Cardiac repolarization abnormalities seen with ketoconazole and terfenadine, not seen with flucon + terfenadine. But since keto, itra and flucon are azoles, concern exists.

² Azole antifungal agents include ketoconazole, fluconazole, itraconazole

I. General

Handwashing before and after patient contact

Gloves for all procedures involving contact with body fluids or moist tissues (diapering excepted) including needle procedures (e.g., venipuncture, injections)

Gowns when visible splash/splatter anticipated

Eye protection (face shield > goggles > glasses) when visible splash/splatter anticipated

Mask when visible splash/splatter or for contact with patient suspected of airborne dissemination. In 1992,

NIOSH recommended that half-mask respirators with HEPA filters always be used (final regulations requiring these are still pending, 6/94). Recent tests of efficacy have shown a surgical mask (Aseptex Sub-Micron Molded Surgical Mask, 1812, 3M) to be 97.5% vs 99.99% for the HEPA Respirator, 9970, 3M (*Am J Inf Cont* 22:65, 1994). Depending upon rules, the former is more practical.

II. Prevention of Needle Injuries

Dispose at site of use in puncture-proof container (not plastic bags)

Do NOT resheath, snip, or perform other post-use manipulation

If using new "safety" needles, ensure adequate training/practice prior to use

III. Tuberculosis Prevention and Control

A. Screening

1. Recommendations for tuberculin testing (with purified protein derivative):

- HIV-infected persons
- Injection drug users
- Prison/jail inmates
- Homeless persons
- Immunosuppressed persons
- Health care workers
- Upon admission to nursing homes, residential care facilities, hospices

2. Procedure and interpretation

Tuberculin test (abbreviation TBnT). The standard is the Mantoux test, 5 TU PPD in 0.1 ml diluent stabilized with Tween 80. Read at 48–72 hours measuring maximum diameter of induration.

- ≥ 5 mm is **positive** in the following: + HIV or risk factors, recent close case contacts, chest x-ray consistent with healed tuberculosis.
- ≥ 10 mm is **positive** in the following: foreign-born in countries of high prevalence, IV drug users, low income populations, nursing home residents, patients with medical conditions which ↑ risk.
- ≥ 15 mm is positive in all individuals (*Am Rev Resp Dis* 142:725, 1990).

Two-stage TBnT: use in individuals to be tested regularly, i.e., health care workers. TBn reactivity may ↓ over time but boosted by skin testing. If unrecognized, individual may be incorrectly diagnosed as recent converter. If 1st TBnT is reactive but < 10 mm, repeat 5 TU in 1 week, if then ≥ 10 mm = +, not recent conversion (*Am Rev Resp Dis* 119:587, 1979).

(Regardless of BCG immunization status; prior BCG does not contraindicate PPD testing unless documented history of an accelerated reaction.)

3. Anergy testing indicated only if results affect clinical care (see Table 2, page 8). Application of 1 of the following intradermally: (See Table 2, page 8)

- Mumps antigen
- Candida antigen
- Tetanus antigen

Any reactivity is considered positive by most experts.

B. INH prophylaxis for PPD positives if no or inadequate prior treatment

1. Not HIV-infected: 9 months INH

- a. All persons with positive PPD < 35 years of age
- b. All recent (within 2 years) PPD converters (after active disease excluded)

2. HIV-infected persons

- a. INH for 12 months
- b. Rifampin plus pyrazinamide for 2 months (under investigation)

3. Multiply drug resistant TB contacts (contact CDC for advice)

C. Active disease

1. Maintain a high index of suspicion! Nearly all outbreaks of nosocomial tuberculosis related to **failure to identify infected patients**. Once isolation implemented, transmission ceases.

2. Suspect tuberculosis:

- Persistent cough
- Fever
- Malaise
- Lymphadenopathy
- Weight loss
- Chest infiltrate

3. Isolate all suspect patients until smear results available or until 2 weeks of treatment with clinical response
 - a. Well-ventilated room (> 6 air exchanges per hour with negative pressure); close doors and windows
 - b. High efficiency masks (disposable particulate respirators) for health care personnel, visitors, other contacts
 - c. Mask patient with leaving room (conventional surgical mask adequate to reduce droplet dissemination)
 - d. Role of UV light/HEPA filter systems not established
 - e. Respiratory precautions for personnel (See *General, masks, above*)
 - f. In triage areas, emergency room, waiting rooms, provide masks to all coughing patients. Some recommend HEPA filters.

IV. Invasive (Surgical or Other) Procedures

Procedure-specific

Barrier precaution for high-risk exposure: double or triple glove, plastic apron, double sleeves, water-resistant shoe covers, face shield

"Sharps" precautions: avoid hand-to-hand passage of sharps (use Mayo tray or emesis basin), "no touch" surgery, minimize needles in the field, coordinate surgical team

Alternative techniques: blunt needles, staples, Bovie cautery

- V. Sterilization and Disinfection: It is imperative that the risk of disease transmission by instruments be negligible. This requires standardized procedures. Following are several guidelines: [for details: 1. *Disinfection, Sterilization and Preservation*, 4th Ed., editor S.S. Block, Lea & Febiger, Philadelphia, 1991; 2. *Am J Inf Cont* 22:19, 1994]

Levels of resistance of microorganisms to germicidal chemicals (level of disinfection required: high, intermediate, low):

Most resistant: bacterial spores (high) > mycobacteria (intermediate) > non-lipid viruses (polio, rhino) (low) > fungi (candida, crypto) (low) > vegetative bacteria (pseudomonas, staph) (low) > lipid viruses (HSV, CMV, hepatitis B, HIV) (low); least resistant

Activity levels of selected procedures/liquid germicides:

Sterilization: steam autoclaving

glutaraldehyde

Disinfection: glutaraldehyde (high to intermediate)

hydrogen peroxide (high to intermediate)

chlorine compounds, 500-1000 mg/L free

chlorine (household bleach is excellent,

inexpensive) (intermediate)

alcohols, 70% isopropyl (intermediate)

phenolic compounds (intermediate-low)

iodophor compounds (intermediate-low)

quaternary ammonium compounds, 0.1-

0.2% (low)

Instrument-related risks of disease

transmission/level of sterilization/disinfection required/comments:

Critical instruments: routinely penetrate skin or mucous membranes during use, e.g.,

needles, scalpel blades: require sterilization

Semicritical instruments: come in contact with intact mucous membranes during use, e.g.,

flexible fiberoptic endoscopes, laryngoscopes,

vaginal specula: require high level disinfection

Noncritical instruments: normally come in contact with intact skin, e.g., blood pressure cuffs,

stethoscopes, ECG electrodes: sterilization/

disinfection between use is not critical, clean if soiled (household bleach)

Environmental surfaces: If soiled: clean, low-level disinfectant, chlorine compounds (household bleach) very active against HIV. Skin antiseptics are NOT appropriate for disinfecting inanimate surfaces!

APIC Guideline for Infection Prevention and control in flexible endoscopy (Am J Inf Cont 22:19, 1994):

Mechanical cleansing (most important step): carry out immediately before secretions dry, alcohol and aldehyde compounds not to be used for mechanical cleaning (coagulate protein):

- When endoscope removed from patient, flush air/water channel for 10-15 seconds. Aspirate detergent through biopsy/suction channel for 10-15 seconds

- External cleansing. Totally immerse in warm water and detergent

- Brush through suction biopsy channel

- Flush each internal channel

- Rinse

Disinfection:

- Totally immerse in 2% glutaraldehyde or other disinfectant of similar potency for not less than 5 min.

- Rinse with water, then dry

Storage:

- After disinfection, rinse each channel with 70% alcohol, dry with compressed air

- Store in hanging position (not coiled in box)

TABLE 21
ALTERNATIVE THERAPIES FOR HIV*

- In the context of HIV infection, the term "alternative" has two different meanings: (a) use of unlicensed and/or unproven agents, (b) alternative acquisition of licensed drugs.
- Early unorthodox treatments included megadose vitamin C, AL-721 (a mixture of lipids extracted from egg yolks with acetone), dinitrochlorobenzene (DNCB) (a topical sensitizer), ribavirin (an antiviral agent effective against respiratory syncytial virus, Hantaan and several arenaviruses) and dextran sulfate.
- Extent of usage of alternative therapies varies but is in the range of 20 to 40% of patients. Hence, care providers at least must be aware of such agents.
- There are many alternative agents; this is a list of ones in common, current use.

AGENT	NATURE OF AGENT	ADVERSE EFFECTS/COMMENTS
GLQ 223 (Compound Q, trichosanthin)	Protein isolated from root tubers of <i>Trichosanthes kirilowii</i> (used in China to induce abortion)	Flu-like symptoms: myalgia and headache (3/4), fever (1/2); rashes (controllable with acetaminophen or NSAIDs). Mental status changes (12%) with coma in several patients. No changes in CD4 noted. Combination studies with zidovudine in progress.
Hypericin (HY), pseudohypericin (PHY)	Polycyclic diones derived from the herb <i>Hypericum triquetrifolium turra</i> (St. John's wart)	Reversible ↑ in liver function tests with OTC preparations. A clinical trial with IV synthetic HY is in progress; photosensitivity is dose-limiting toxicity.
Oral alpha interferon (Kemron)	Immunomodulator, antiviral agent; given in oral form	Rare nausea. North American trials unable to confirm positive Kenyan results. No impact on CD4 cells, symptoms or disease progression seen in placebo-controlled studies.
Cysteine precursors (N-acetyl cysteine, NAC; OTC)	Cysteine precursor, used for mucolytic rx in bronchitis and systemically for acetaminophen poisoning	Minimal toxicity. Phase I NIAID study shows minimal oral bioavailability; no change in CD4, p24 antigen, plasma viremia or cysteine levels.
Pentoxifylline	Trisubstituted xanthine, FDA-approved for claudication	Action: inhibits tumor necrosis factor (TNF). TNF levels ↑ with progression of disease and wasting syndrome. For approved indications, occasional GI, CNS disturbances. Preliminary trial results inconclusive to date (<i>Clin Inf Dis</i> 18:285, 1994).
Peptide T	Synthetic 8-amino acid peptide mimics vasoactive intestinal peptide (VIP). Antiviral and nervous system activities postulated.	No toxicities via inhaled route. Reports of improved dementia and neuropathy being studied in ongoing trials.

* Adapted from D.I. Abrams, *Medical Management of AIDS*, 4th Edition, Eds.: M.A. Sande, P.A. Volberding, W.B. Saunders & Co., 1994

TABLE 22
AIDS INFORMATION AND REFERRAL SERVICES

- AIDS/HIV Clinical Trials conducted by National Institutes of Health and FDA-approved efficacy trials: 1-800-874-2572
- For a wide variety of AIDS/HIV information, resources, publications, call the National AIDS Clearinghouse: 1-800-458-5231
- To find out about AIDS resources in your area, call the National AIDS Hotline: 1-800-342-2437
- The AIDS/HIV Treatment Directory is published by the American Federation for AIDS Research (AmFAR) and is updated quarterly: 733 Third Ave., 12th Floor, New York, NY 10017-3204. Telephone: (314) 731-4554

COMPASSIONATE USE/TREATMENT/EXPANDED ACCESS PROGRAMS

INDICATION	AGENT	MANUFACTURER	TELEPHONE
AIDS or advanced ARC, who have failed or intolerant of ZDV	ddC d4T (stavudine)	Hoffmann-La Roche Bristol-Myers Squibb	(800) 332-2144 (800) 842-8036
HIV disease who have failed or intolerant of other approved therapies	3TC	Glaxo	(800) 248-9757
Cryptosporidiosis	Albendazole Azithromycin Diclazuril	Smith-Kline Beecham Pfizer Janssen Pharmaceutica	(800) 366-8900 (203) 441-6148 (800) 521-AIDS
Fungal infections: Failure on approved rx Children, serious mycoses	Itraconazole Fluconazole	Janssen Pharmaceutica Pfizer	(609) 730-3118 (203) 441-4162
Mucocutaneous herpes simplex, acyclovir-resistant	Foscarnet	Astra	(800) 388-4148
Mycobacterium avium-intracellulare (failed or intolerant of current agents)	Azithromycin	Pfizer	(203) 441-5941
Toxoplasmosis, CNS	Azithromycin	Pfizer	(203) 441-5701

TABLE 23
DIAGNOSTIC AND LABORATORY PROCEDURES FOR THE CLINICIAN

Induced Sputum for Identification of Pulmonary Pathogens, Sputum Collection (Ng *et al.*, *Arch Path Lab Med* 113:488, 1989):

- (1) No solid food for 8 hours
- (2) Immediately before induction: vigorously brush teeth, gingival margins, tongue and buccal surfaces with water or saline. Rinse thoroughly. Gargle several times with water.
- (3) Inhale aerosol solution of 3% saline generated by ultrasonic nebulizer (DeVilbiss Model 35B or UltraNeb-100) for 20 minutes (3 to 7 ml/minute)
- (4) Expectorate one specimen during the first few minutes of inhalation and the second during the remainder of the procedure. Label each. The second is more likely to be representative of distal respiratory tract secretions. Examine the first only if the second is non-diagnostic.

GRAM'S STAIN:

- (1) Transfer small quantity of specimen to clean glass slide, spread over area about size of dime, air dry, then heat "fix" by passing quickly through burner flame 3 times (do not overheat!)
- (2) Using 8-10 drops of gentian violet solution, cover heat-fixed smear. Allow to stand 1 minute, then rinse with gentle flow of water.
- (3) Cover smear with 8-10 drops of Gram's iodine solution, stain for 1 minute, then rinse with water as in (2)
- (4) Holding slide at angle (over sink), apply drops of 95% ethyl alcohol, gently agitate until no more blue runs off
- (5) Add 8-10 drops of safranin solution for 30 seconds, then rinse with water, gently blot dry and examine under microscope (oil immersion)

WRIGHT-GIEMSA STAIN: It is easiest to use Camco Quik Stain II (Baxter), which is a buffered Wright-Giemsa stain. Prepare blood smear, allow to dry. Then dip slide in stain for 10 seconds, remove and dip slide in distilled water for 20 seconds. Remove, dry, and examine microscopically.

ACID-FAST STAIN (Kinyoun's Method) (Fisher Diagnostics AFB Stain Kit): Prepare slide as with Step 1 for Gram's stain. Then stain slide with carbol fuchsin solution for 3 minutes (do not heat). Wash gently in running water. Rinse with decolorizer until no more color appears in washings (about 2 minutes). Wash again in running water. Counterstain with brilliant green stain for 30 seconds. Wash again, air dry, and examine microscopically (oil immersion).
Cryptosporidia: Use Kinyoun carbol-fuchsin reagent. Decolorizer is 1% sulfuric acid rather than 0.5% as used for mycobacteria.

INDIA INK PREPARATION (Cerebrospinal fluid):

- (1) Centrifuge the CSF at 2000 x G for 10 minutes. The resulting sediment is used for microscopic examination.
- (2) Place 2 loopfuls of India ink on a clean glass slide
- (3) Add 1 drop of the CSF sediment and mix. The preparation should be brownish in color (not black).
- (4) Cover with a coverslip and examine under low- and high-power dry magnification. *C. neoformans* will reveal budding yeast cells surrounded by a clear halo. WBCs may show a halo but the halo has a fuzzy irregular edge.

KOH PREPARATION FOR FUNGI: Mix specimen (pus, tissue) with a drop of 10-20% KOH solution on a clean slide. Cover with a clean coverslip, and press gently to make a thin mount. Gentle warming may aid in clearing. Scan under low power with reduced light for fungal elements.

TABLE 24
LIST OF GENERIC AND COMMON TRADE NAMES

GENERIC NAME	TRADE NAME	GENERIC NAME	TRADE NAME	GENERIC NAME	TRADE NAME
Acyclovir	Zovirax	Flucytosine	Ancobon	Primaquine	Primaquine
Amikacin	Amikin	Foscarnet	Foscavir	Pyrazinamide	Pyrazinamide
Amphotericin B	Fungizone	Ganciclovir	Cytovene	Pyrimethamine	Daraprim
Atovaquone (566C80)	Mepron	Human growth hormone (rHGH)	Protoprin	Ribavirin	Virazole
Azithromycin	Zithromax	Imipenem	Primaxin	Rifabutin	Mycobutin
Bleomycin	Blenoxane	Interferon alfa	Roleron-A, Intron A	Rifampin	Rifadin
Capreomycin	Capastat	Iodoquinol	Yodoxin	Saquinavir (Ro 31-8959)	
Ciprofloxacin	Cipro	Isoniazid	INH, Laniazid, Tubizid	Sargramostim (GM-CSF)	Leukine, Prokine
Clarithromycin	Biaxin	Itraconazole	Sporanox	Thiacetazone	Tibione
Clindamycin	Cleocin	Ketoconazole	Nizoral	Trimethoprim	Proloprim, Trimplex
Clofazimine	Lamprene	Lamivudine (3TC)		Trimethoprim/ Sulfamethoxazole	Bactrim, Septra
Cycloserine	Seromycin	Megestrol	Megace	Trimetrexate	Neutrexin
Stavudine (d4T)	Zerit	Norfloxacin	Noroxin	Vidarabine	Vira-A
Didanosine (ddI)	Videx	Ofloxacin	Floxin	Vinblastine	Velban
Doxorubicin	Adriamycin	Paromomycin	Humatin	Vincristine	Oncovin
Dronabinol	Marinol	Pentamidine	Pentam 300	VP16	VePesid
Erythropoietin	Epogen, Procrit	Pentamidine aerosol	NebuPent	Zalcitabine (ddC)	HIVID
Ethambutol	Myambutol	Podofilox	Condylox	Zidovudine (ZDV)	Retrovir
Ethionamide	Trecator	Podophyllum/ benzoin	Podocin 25, Pododerm, Podofin		
Etoposide	VePesid				
Fligrastrim (G-CSF)	Neupogen				
Fluconazole	Diflucan				

TRADE NAME	GENERIC NAME	TRADE NAME	GENERIC NAME	TRADE NAME	GENERIC NAME
Adriamycin	Doxorubicin	Lamprene	Clofazimine	Protoprin	Human growth hormone (rHGH)
Amikin	Amikacin	Leukine	Sargramostim (GM-CSF)	Retrovir	Zidovudine
Ancobon	Flucytosine	Marinol	Dronabinol	Rifadin	Rifampin
Bactrim	TMP/SMX	Megace	Megestrol	Rimactane	Rifampin
Biaxin	Clarithromycin	Mepron	Atovaquone	Roleron-A	Interferon alfa
Blenoxane	Bleomycin	Myambutol	Ethambutol	Septra	TMP/SMX
Capastat	Capreomycin	Mycobutin	Rifabutin	Seromycin	Cycloserine
Cleocin	Clindamycin	NebuPent	Pentamidine aerosol	Sporanox	Itraconazole
Cipro	Ciprofloxacin	Neupogen	Fligrastrim (CSF)	Tibione	Thiacetazone
Condylox	Podofilox	Neutrexin	Trimetrexate	Trecator	Ethionamide
Cytovene	Ganciclovir	Noroxin	Norfloxacin	Trimplex	Trimethoprim
Daraprim	Pyrimethamine	Oncovin	Vincristine	Velban	Vinblastine
Diflucan	Fluconazole	Pentam 300	Pentamidine	VePesid	Etoposide (VP16)
Epogen	Erythropoietin	Primaxin	Imipenem + cilastatin	Videx	Didanosine (ddI)
Floxin	Ofloxacin	Procrit	Erythropoietin	Virazole	Ribavirin
Foscavir	Foscarnet	Prokine	Sargramostim (GM-CSF)	Yodoxin	Iodoquinol
Fungizone	Amphotericin B	Proloprim	Trimethoprim	Zithromax	Azithromycin
HIVID	Zalcitabine (ddC)			Zerit	Stavudine (d4T)
Humatin	Paromomycin			Zovirax	Acyclovir
Intron A	Interferon alfa				

- A**
- Acalculous cholecystitis **40**
- Acanthamoeba **51**
- Acid-fast stain **112**
- Acyclovir 22, 30, **31**, 33, **37**, 41, 53, 55, 72, 73, **79**, 82, 88-90, 94, 102, 104-106, 111, 113
- Addison's disease 27, **28**, 75
- Adrenal 26, 27, **28**, 74
- AIDS dementia complex **21**, **54**
- Amikacin **59**, 60, **76**, 82, 94, 99, 107, 113
- Amphotericin B 14, 26, 49, 53, 62, **64-66**, **74**, 82, 90, 94, 100, 103-107, 113
- Anemia 17-19, **38**, **39**, 45, 68, 71, 73-75, 77-79, 81, 85, 88, 96
- Anergy **8**, **11**, 58, 109
- Anxiety 21, **53-55**, 95
- Arthritis **48**
- Aspergillosis **46**, **64**
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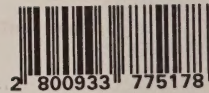
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UAB Mini Park

Sponsored by
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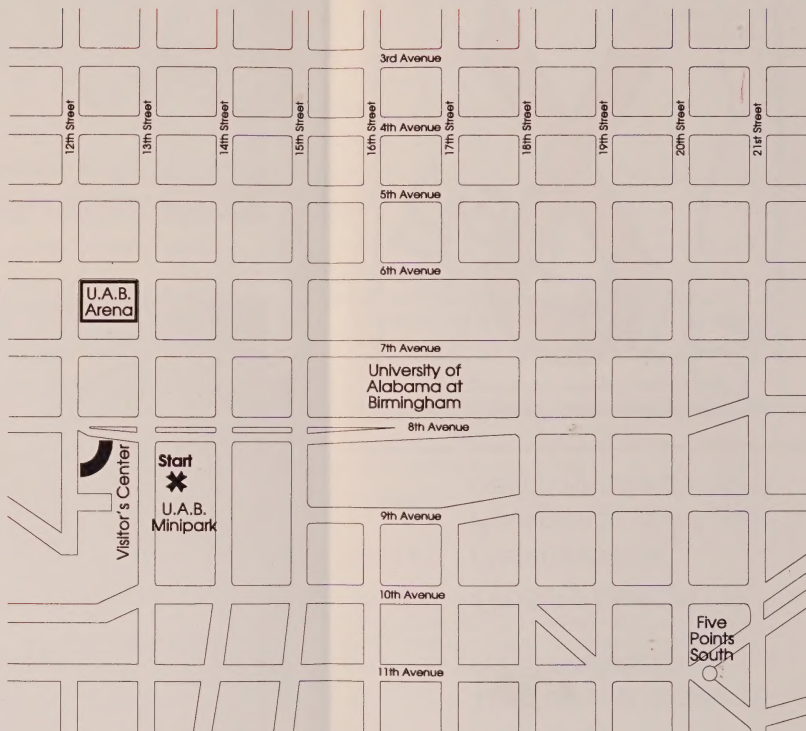
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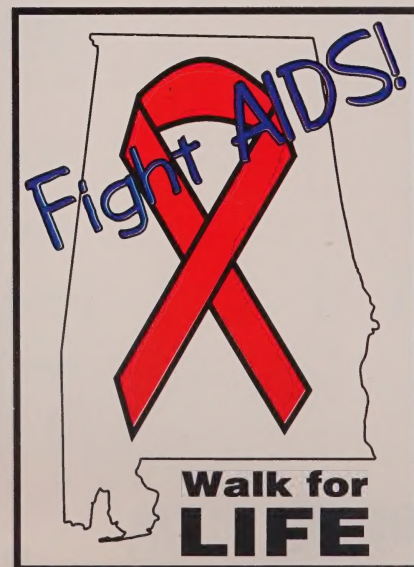


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- 1:00** *Registration Opens*
Food Vendors Open
Entertainment Begins
- 3:00** *Opening Ceremony*
(Promptly)
Third Annual Alabama
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- 4:30** *Closing Ceremony*
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\$100	T-Shirt
\$250	Cooler
\$500	Sports Bag
\$1000	Jacket



Merchandise photo courtesy Jim S. Roe

And...

For the individual who turns in the most money on the day of the walk:

Grand Prize!!!

For the person who raises the most money for the Birmingham AIDS Outreach AIDS Walk, that person and a companion will receive:

- 2 Round-Trip Airline Tickets to the city of choice in the continental United States.
- 3 nights First Class Hotel accommodations.
- All hotel taxes and service charges



* Air tickets are via USAir. Please check USAir guide for cities served from Birmingham. Certain blackout dates and other restrictions apply. A minimum of 21 days notice is necessary for travel.

3rd Annual Alabama
AIDS Walk

1994 REGISTRATION FORM

Yes!

I want to team up with my friends and walk to fight AIDS.

Mail or fax this form to: AIDS Walk, P.O. Box 550070,
Birmingham, AL 35255
Fax (205) 322-2131

Please Print

Name _____

Address _____

City _____ State _____ Zip _____

Phone: Work _____ / _____

Home _____ / _____

Organization/Club/School _____

I am unable to walk, but will make a donation of
\$ _____ (please enclose check payable to
Birmingham AIDS Outreach)

Age _____ Sex: ☐ M ☐ F

Have you walked in a walk before? ☐ Yes ☐ No

If yes, when? _____

Send Me

- ☐ Brochures (Send me _____ copies)
- ☐ An article to include in my corporate newsletter
- ☐ Information on HIV/AIDS support programs
- ☐ Posters - I'll put them up at work

Employer _____

Team AIDS Walk

Team Captain _____

Team Name _____

Company Name _____

I need _____ additional entry forms for other team members
(each team member must complete a separate form).

Volunteers Needed

- ☐ I'm unable to walk, but would like to volunteer.
- ☐ I am walking but would also like more information on volunteering before and after the walk.

Who Benefits?

Proceeds from the Walk will go to the following agencies:

A Baby's Place
Agape House
AIDS Coalition of Huntsville
AIDS in Minorities (AIM)
AIDS Services Center of Anniston
AIDS Task Force of Alabama (ATFA)
AIDS Support Awareness Programs
Birmingham AIDS Outreach (BAO)
Castlehill Clinic (AIDS Clinic – Tuscaloosa)
Lee County AIDS Outreach
Mobile AIDS Support Services (MASS)
Montgomery AIDS Outreach (MAO)
St. George's Clinic
UAB 1917 Clinic
UAB AIDS Research Center
UAB Children's Hospital Family Clinic
West Alabama AIDS Outreach
Wiregrass AIDS Outreach
VA Hospital AIDS Clinic

And other AIDS organizations within the state of Alabama.

3rd Annual Alabama

AIDS Walk

1994 Local Sponsors

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AIDS WALK

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Birmingham, AL
Permit No. 90

*For people who like to have fun,
stay fit, and help their community:*

**You can walk for
AIDS education,
care and services!**

The 3rd annual Alabama

AIDS Walk



Sponsored by Birmingham AIDS Outreach

Take to the Streets...Against AIDS

Put on your walking shoes and join us for the Birmingham AIDS Outreach...

1994 Alabama AIDS Walk...

We're expecting a huge crowd at our starting line and you and your team can be part of it all!

Get fit, have fun, FIGHT AIDS

1. Register Today...

Fill out the attached registration form. Send it in or fax it and we'll send you your official AIDS Walk registration packet.

2. Start Your Legwork...

Talk to your friends, family, neighbors, classmates, coaches and coworkers. They may know someone living with HIV or they may want to walk in honor of someone who has died from AIDS. Any five or more people can walk together as a team. *Start forming your team NOW.*

3. Advance Warm-Up...

Collect your team pledges in advance. Your employers, local businesses, generous friends and neighbors will probably be glad to support you every step of the way toward fighting AIDS.

4. On Your Mark...

Step up to the starting line. We'll walk rain or shine! Meet us at the UAB Mini-Park on Sunday, October 23. There will be food and entertainment for everyone.

**For more information
call the AIDS Walk Hotline
(205) 322-4197**



1994 Registration Form

Yes!

I want to team up with my friends and walk to fight AIDS! Please send my walker information packet.

Mail or FAX this card to: AIDS Walk, P.O. Box 550070,
Birmingham, AL 35255 FAX (205) 322-2131

Please print.

Name _____

Address _____

City _____ State _____ Zip _____

Phone: Work () _____

Home () _____

Organization/Club/School _____

I am unable to walk, but will make a donation of
\$ _____ *(please enclose check payable to*
Birmingham AIDS Outreach)

Age _____ Sex : M _____ F _____

Have you walked in a walk before? Yes _____ No _____

If yes, when? _____

Send Me:

_____ Brochures (Send me _____ #)

_____ An article to include in my corporate newsletter

_____ Information on HIV/AIDS support programs

_____ Posters...I'll put them up at work

Employer _____

Team AIDS Walk

Team Captain _____

Team Name _____

Company Name _____

Please indicate if you need additional registration forms for other
Team Members (each team member must complete a separate
form). I need _____ additional entry forms.

Volunteers Needed

_____ I'm unable to walk, but would like to volunteer.

_____ I am walking but would also like more information on
volunteering before and after walk.

Walk with us so others
won't have to walk
alone...

Register today...and
bring a friend



You can walk for AIDS
education, care and services!

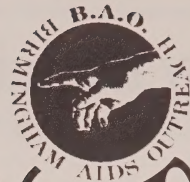
The 3rd annual Alabama

AIDS Walk

Sunday October 23, 1994
UAB Mini Park



The Outreach



VOLUME 7, NO. 2 OCTOBER, 1994

3rd Annual AIDS Walk...

BAO TAKES TO THE STREET!

Alabama AIDS Walk 94

"For All Walks Of Life"

Live entertainment, fun, prizes, children's activities, food and drink!



Birmingham AIDS Outreach
Sun., Oct. 23
Call (205) 322-4197

Mobile AIDS Support Services
Sun., Oct. 30
Call (205) 433-6277

BAO volunteers and donors will be taking to the streets of southside in record numbers on Sunday 23 October for the third annual AIDS Walk. This event, traditionally one of BAO's most important fund and consciousness-raising activities, is scheduled to begin promptly at 3 pm at the UAB Minipark

(on University Boulevard between 13th and 14th streets). Registration and entertainment will begin at noon at the park. All activities will take place rain or shine.

Though people from all over the state have already volunteered, pledged, and signed up in unprecedented numbers, BAO is still seeking contributions of time, effort, expertise and/or money in order to make the day a real success in the continuing fight against HIV, AIDS and ignorance. You and your friends and co-workers can help in this effort while having fun and keeping fit at the same time. Just a few hours out of your Sunday afternoon can make a

real difference! You might even win a great prize (courtesy of Marco Polo of the Carlson Travel Network): the participant raising the most money for BAO will receive 2 round-trip airline tickets to the continental U.S. city of their choice plus 3 free nights of first class hotel accommodations in that city.

In addition, there will be other prizes and premiums to be awarded at the 4:30 pm closing ceremonies.

If you would like to walk or to volunteer for other duties associated with this exciting event or if you would like to be a financial sponsor, please contact the BAO office at (205) 322-4197. Talk to your friends, family, neighbors, classmates and co-workers. Perhaps a group may want to walk in memory of someone who died from AIDS or in honor of someone living with the disease. Any five or more people can walk together as a team. There is no more meaningful way to stand up and be counted!

A SCENE FROM 1993's WALK:



PHOTO BY BRAD DALE

Say it again, Sam...

A MESSAGE FROM THE EXECUTIVE DIRECTOR



Short Stuff

ONGOING NEEDS FOR CLIENTS

Paper Products

*napkins, kleenex, towels, etc.

Canned Goods

*soups & vegetables
*fruit
*meats (small canned hams, tuna, chicken, salmon, beef stew, etc.

Boxed Goods

*instant breakfast
*cereals
*rice
*macaroni & cheese
*crackers
*hamburger helper
*pasta
*powdered milk

Bottled Goods

*cooking oil
*Gatorade
*fruit juices
*jellies & jams
*cold drinks
*condiments
*spaghetti sauce

SPECIAL NEEDS

*FANS
*AIR CONDITIONERS
*MICROWAVES
*TELEVISION SETS
*VCRs
*LAPTOP COMPUTER

YOUR CONTRIBUTION TO BAO IS WELCOME.

PLEASE MAIL TO P.O. BOX 550070,

BIRMINGHAM, AL 35255-0070.

IF YOU HAVE QUESTIONS,

CALL 322-4197 MONDAY THRU

FRIDAY, 9:00 AM TO 6:00 PM.

AIDS AND FAMILIES

Birmingham AIDS Outreach and Children's Aid Society are collaborating on a project to address the growing crisis of AIDS orphans in Alabama. Current estimates in this country put the number of children who have lost their parents to this epidemic at 80,000-120,000. In Alabama the problem is growing. This state has the highest rate of infection in women in the country (double the national average) and one of the highest rates among heterosexuals (also double the national average). Alabama has one of the highest rates of new HIV infections in the country. Losing a parent is a traumatic experience for anyone, especially the very young. We need to work to ease this pain.

Family Pairs, a program developed by the BAO Social Services Committee and Children's Aid Society addresses these issues. Family Pairs will train a resource family to "pair" with the family affected by HIV. If relatives are available, they will be utilized first. Families are provided Foster Parent Training by Children's Aid Society and HIV/AIDS Training by BAO. If no relatives are available, a pool of trained resource families will be available and paired with the HIV affected family. An opportunity for the child(ren) of the HIV affected family to bond with the resource family is provided.

The goals for the first year include recruiting twenty potential families and training at least fifteen of them to serve as resource families. The theme for World AIDS Day 1994 is **AIDS and Families**. This project needs your help. We need resource families and funds to recruit, train and prepare home studies. If you are interested in becoming a resource family or in providing funding for this project, you can contact Teresa Coker at Children's Aid Society, (205) 251-7148 or me at BAO, (205) 322-4197. This is a new initiative that is desperately needed in Alabama. Please help us care for the children in our state.



JIM FOLSOM
GOVERNOR

STATE OF ALABAMA
GOVERNOR'S OFFICE
MONTGOMERY 36130

September 28, 1994

Birmingham AIDS Outreach
205 32nd Street South
Birmingham, Alabama 35203

Dear Grantee:

As Governor of Alabama, I am pleased to congratulate you on your Alabama AmeriCorps program. Your exceptional work will help Alabama communities and will educate a new generation of servant leaders for our state.

I offer you the support and resources of my Office on National and Community Service. Also, I send my very best wishes for success as you "get things done" to improve the lives of the citizens of Alabama.

Again, thank you for your commitment to community service and to the future of our state.

With warmest personal regards, I remain

Sincerely,

Jim Folsom
Governor

JF/tk

Cather Appointed Newsletter Editor by BAO.



Birmingham Aids Outreach recently announced the appointment of southside resident Patrick Cather as new editor of BAO's newsletter, **The Outreach**. According to BAO, Cather's appointment will enable **The Outreach** to achieve its goal of becoming an increasingly important medium for disseminating on a regular schedule news and other vital information about the AIDS epidemic in Alabama.

The new editor, a local rare book and art dealer, has an extensive printing and publishing background and formerly served as editor of the UAB student newspaper, **The Kaleidoscope**. During the last fifteen years, he has written and published extensively on such topics as the arts in Birmingham, jazz and blues, Alabama history and bibliography, and librarianship. **Birmingham Bound**, a critical survey of the most important books about Alabama's largest city, is his most recent effort. It is available locally from Smith and Hardwick Books and the author is donating to BAO \$5.00 for each copy sold in Birmingham.

A former professional musician, the new editor was elected to the Alabama Jazz Hall of Fame in 1991. An avid art collector, he serves on BAO's "You Gotta Have Art" auction committee and is a volunteer for the upcoming AIDS Walk. In addition, he is a member of the Birmingham Art Association, the Birmingham Museum of Art, the Alabama Society of Archivists, the Cahaba River Society and the ACLU of Alabama.

As to his objectives for **The Outreach**, Cather says he wants to increase its frequency and circulation and that, "While being aware of the fact that **The Outreach** is primarily a communications educational, and public relations vehicle for BAO, I do plan to open it up a bit to constructive feedback from the community." Cather added that he welcomed "this opportunity to increase my efforts on behalf of BAO. Those of us in the community not yet directly affected by HIV can't afford to be smug about the epidemic." Those with ideas as to making the newsletter more responsive are asked to communicate those ideas to the new editor, care of Birmingham AIDS Outreach, P.O.Box 50070, Birmingham, Alabama 35255.

The new editor, who is single, lives in the Forest Park neighborhood with his two dogs, "a humane society graduate named Jose and a Jack Russell terrier known for some reason as Peigan."

ADRIAN DANIELS MEMORIAL HOLIDAY GIFT BOX PROJECT

Adrian Daniels was a beloved former BAO staff member and director who died of AIDS complications on 27 April 1994. His strength, courage and humanity touched many lives. To acknowledge that fact, BAO's board of directors recently voted to designate the organization's annual gift box program as the "Adrian Daniels Memorial Holiday Gift Box Project."

As traditional winter holidays approach, volunteers at BAO have begun collecting contributions for this yearly effort. Of all of BAO's programs, this is perhaps the one bringing the most joy to our clients, volunteers and staff.

Your help is needed in making the holidays a wondrous and fun-filled time for our clients. BAO needs volunteers to solicit and organize contributions, to assemble and

decorate the gift boxes and to deliver the gifts.

Further, we need the following new items to be donated by Wednesday 14 December to be included in the gift boxes: gift certificates; canned & baked goods; toiletries; household cleaners & supplies; paper products such as kleenex & paper towels; all types of clothing; and stocking stuffers such as books, calendars, decorations, small games & candy.

The boxes will be put together on Wednesday 21 December and then delivered on Thursday and Friday, the 22nd and 23rd. Please join us in making the upcoming holiday season a special time for our clients...and yourself. Call the BAO offices at 322-4197 for more information.

BAO Statistics for August:
 Active client caseload: 254
 Clients served: 139
 Lost to follow-up: 6
 Deaths: 10
 New clients: 16
 Reactivated: 3
 Financial assistance to clients: \$8,743
 Year to date: \$102,096

NEW!

"LET'S LIVE"

A new, no-fee support group for all healthy HIV+ individuals.

Meets Tuesdays from 5:30-7:00 pm at 956 Montclair Rd., Suite 112.

Led by George C. James, PhD, Grayson & Assoc.

For details call 939-0017

Discretion and anonymity assured. All calls answered by HIV+ individuals.

Really hot dates

CALENDAR OF EVENTS

Monday Night Support Group

6:30pm to 8:00pm

For parents, family members
& loved ones of people
living with HIV/AIDS

Tuesday Night Support Group

6:30pm to 8:00pm

For people living with
HIV/AIDS, their family
members & loved ones

Wednesday Night Support Group

(except the last Wednesday
night of the month)

6:30pm to 8:00pm

For people living with
HIV/AIDS

Last Wednesday Of Each Month

Positive Attitudes Group

6:30pm, free dinner

7:30pm, free presentation

Friday Mornings

Women's Support Group

10:00am 'til noon

October 23

Annual AIDS Walk

Noon 'til 5:00 pm

December 1

World AIDS Day

Events to be announced

December 4

Annual Art Auction

Annual Benefit Auction Planned...

YOU GOTTA HAVE ART!

BAO's 4th annual "You Gotta Have Art" benefit auction will take place from 3 to 6 pm on Sunday 4 December at Space One Eleven Art Center, 2409 2nd Avenue, North (downtown). This BAO-sponsored event has become one of the cultural high points of the late fall season in Birmingham and is always eagerly anticipated by those hoping to add to their collection a choice piece by a favorite artist while financially benefiting BAO's programs at the same time. The art auction committee, chaired by Jeff Barton, promises that this year's auction will be the best yet.

Though some of the contributed works will be on display in the windows at Space One Eleven throughout the month of November, BAO will accept donated pieces up until 28 November at which time the entire exhibit for the auction will be set up inside the gallery. BAO solicits help from anyone in adding suitable artworks to the auction. If you wish to contribute something to be sold for the organization's benefit, please call Birmingham AIDS Outreach at 322-4197.

Among the artists who have already agreed to participate are such luminaries as Beth Bethard-Hill, Jim Burnett, John Dillon, Larry Anderson, Sara Armstrong, Katherine Chew, Maud Corier-Belser, Charles Collins,

Lane Cooper-Lowrimore, Paul DeCarlo, Beverly Erdreich, Jean-Jacques Gaudel, Martha Hopkins, Sally Johnson, Armor Keller, Janice Klunge, Cam Langley, Denise Lee, Cordray Parker, Billy Renkl, Joy Russell, Amasa Smith, Scott Stephens, Chip Stinson, Judith Taylor-Rogers, Louise West, Barbara Evans, Michael Meads, Howard Cruse, Catherine Cabaniss, Todd Curren, Ben Scokel, Richard Wood, Lee Woehle, Florence Coles and Anne Arrasmith. The editor regrets that deadline considerations prevent him from publishing a complete list in this issue of **The Outreach** but all donations are needed and appreciated. A full listing will appear in the next issue of **The Outreach**.

According to Jeff Barton, "The excitement with which contributing artists have given of their time and talents is a true tribute to the generosity of our local arts community."

Please note that BAO does not limit itself to accepting only contributions from artists. The collectors and gallery owners among the readership of **The Outreach** are also urged to donate worthwhile pieces to the benefit. In some cases there may be tax advantages to those individual collectors who contribute. Check with your accountant and then call BAO at (205) 322-4197 for more details as to how you can help in this cause.

Purchases at the auction may be paid for by cash, check or credit card. An informal reception with food and drink will begin at 3 pm. Mark your calendars to attend this very special event!

YOU GOTTA HAVE ART!

AMERICORPS IS HERE!

AmeriCorps members have a goal: getting things done. AmeriCorps is a national program designed to engage thousands of Americans of various ages and backgrounds in a domestic service operation akin to the Civilian Conservation Corps of the 1930s.

AmeriCorps at Birmingham AIDS Outreach will be the first such program in Alabama and among the first in the country. BAO AmeriCorps members will be an important part of the front-line team of AIDS caregivers in the United States. Members will be engaged in the vital task of providing home health care for people with AIDS.

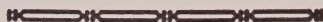
An important part of the AmeriCorps program is that while members work in their communities, they can also prepare for their own future. A living allowance and health care benefits are provided for each member. In addition, for each year of completed service, AmeriCorps members will receive an educational award which they can use to pay for education or to repay past school loans. Further, no interest will accrue on student loans while members are in AmeriCorps service.

The living allowance for participants is \$7662 yearly with an annual educational award of \$4725 for full-time service and \$2362 for part time service.

For more information about this important new program contact Terry Gunnell, AmeriCorps director, BAO, P.O.Box 550070, Birmingham, Alabama

35255 or call Terry at (205) 322-4197. The e-mail address is BAIDSO@aol.com.

-reprint from the
Alabama Forum.



News You Can Use...

SIMPLE TIPS TO KEEP PETS AND OWNERS SAFE & HEALTHY by Susan Rodgers

The saying goes, "Man's best friend is a dog." It doesn't mention cats, birds, rabbits or fish which are just a few of the "best friends" people have these days. Pets have that special ability to give unconditional love and acceptance - qualities that are not as easy to find in human relationships.

While pets generally don't pose a disease problem for most people, HIV makes pet owners more susceptible to all kinds of diseases, including zoonoses.

Zoonoses refers to diseases that can be contracted by humans from other animals. Current evidence supports the fact that pets pose a minimal risk. Monkeys, stray or sick animals, and exotic or wild animals have been found to be more likely to carry diseases that could spread to humans.

There are a few guidelines people with HIV disease should be aware of when caring for pets:

- *Keep pets clean and well groomed (with nails trimmed);

- *Control fleas on your pet;

- *Avoid bodily fluids: vomit, feces, urine and saliva; don't let your pet lick any wounds you might have;

- *Place your cat's litter box away from the kitchen and sleeping areas; if possible have someone who is not HIV infected clean the box; use disposable liners and change them each time you change the litter; disinfect the litter box at least once a month by filling it with boiling water and letting it stand for five minutes;

- *Take your pet for an annual checkup; at the first sign of sickness, contact your veterinarian.

To prevent your pet from acquiring diseases which can be passed on to humans,

- *Feed your pet commercial pet foods; never feed pets raw meat or unpasteurized milk; don't let your pet eat its own or other animals' feces;

- *Keep your pet from drinking from the toilet bowl or rooting through garbage;

- *Prevent your pet (especially cats) from hunting; cats can catch toxoplasmosis from eating birds and rodents; if your cat must go outdoors, put a double bell on it's collar to help scare away potential prey;

- *Keep your dog on a leash during walks to control scavenging.

For more information on zoonoses, safe pet guidelines or to get information regarding specific pets, contact PETS, 1747 Connecticut Avenue, NW, Washington, DC 20009 or call (202) 234-PETS.

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BIRMINGHAM AIDS OUTREACH
P.O. BOX 550070
BIRMINGHAM, AL 35255-0070



A Note From Your Editor...

ANGELS IN ATLANTA ...AND ELSEWHERE

On Sunday 18 September I rode with friends to Atlanta to attend the Alliance Theatre Company's production of Tony Kushner's monumental *Angels in America: Millennium Approaches*. Even though I had seen the brief excerpts broadcast on PBS about a year ago and had subsequently read the book, I was totally unprepared for what proved to be my most moving and exciting theater experience since I saw my first opera in New Orleans 27 years ago. There was, of course, a full house made up of male and female, straight and gay, young and old, black and white and all shades in between. The play spoke to ALL

of us on themes of sex, politics, AIDS, love and responsibility. This collection of themes has been done before but I think no playwright has ever been as artistically successful as Kushner at actually bringing the effort to a triumphant fruition. The dramatic cliffhanger ending found me wanting to stay in my seat until next year when the Alliance will produce Part II of the play. Even the **Birmingham News** was left with no viable choice but to give the production a four star review!

A national touring company production is in the process of taking the play to 20 American cities. I strongly urge you to make every effort to see *Angels*...

As this is my first issue of **The Outreach**, it seems appropriate that I should extend "thanks" to Sam Thompson for giving me this opportunity to use whatever talents I have for a worthy cause. I would also like to thank Bob Burns, Cindy Nelms, Perry Schwartz and Joy Godsey for collectively involving me more with BAO's mission. It's good to realize that both Birmingham and Mobile have their "angels" too!

-Patrick Cather

HELP RAISE AIDS AWARENESS IN OUR COMMUNITY

ORDER YOUR AIDS AWARENESS CHECKS TODAY!!

AIDS AFFECTS EVERYONE



Pay to the
Order of _____

\$ _____

Dollars

Memo _____



GET INFORMED • GET INVOLVED • CARE

12 _____

BIRMINGHAM AIDS OUTREACH RECEIVES A PERCENTAGE OF EVERY ORDER

THE AWARENESS CHECK COMPANY IS A NONPROFIT ORGANIZATION
WHOSE PROCEEDS ARE DONATED TO AIDS ORGANIZATIONS FOR MORE
INFORMATION CALL OR WRITE:

Awareness Check Company
1036 Lindbergh Dr.
Atlanta, GA 30324
PHONE/FAX: 404 841-6112

THIS PROJECT IS A JOINT EFFORT BETWEEN BIRMINGHAM AIDS OUTREACH AND THE AWARENESS
CHECK COMPANY. OUR ORGANIZATION WILL RECEIVE AT LEAST 30% OF EVERY ORDER THAT IS
GENERATED BY OUR SUPPORTORS SO PLEASE SHARE THIS ORDER FORM WITH YOUR FRIENDS,
FAMILIES, CO-WORKERS OR ANYONE ELSE WHO LIKES THEM. EVERY ORDER DIRECTLY HELPS OUR
ORGANIZATION AND HELPS RAISE AWARENESS AT THE SAME TIME.

W E A L L N E E D T H E M W H Y N O T M A K E Y O U R S
S A Y S O M E T H I N G ?

NAME: _____ PHONE: _____ START CHECKS AT NUMBER: _____

ADDRESS: _____

HOW TO ORDER:

Enclose the following in an envelope:

1. A voided check from your existing supply
2. A deposit slip from your existing supply.
3. This order form, completed and totalled.
4. Your payment check made payable to:

AWARENESS CHECK COMPANY
1036 Lindbergh Dr. NE
Atlanta, Ga 30324

SINGLE CHECKS
\$14.95
(PER BOX OF 200)

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CHECKS
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(per box of 150)

_____ boxes @ \$ _____ = _____

☐ Single ☐ Duplicate
Alternate Lettering, Add \$2.00 = _____

☐ Script ☐ Old English

Shipping/Handling = 1.50

Priority Mail \$4.00 = _____

GRAND TOTAL = _____

ALL CHECKS ARE
PRINTED ON
RECYCLED PAPER
AND ARE
PRINTED WITH
SOY BASED INK.



ORGANIZATION IDENTIFICATION
CODE: 027



P.O. BOX 550070
BIRMINGHAM,
ALABAMA 35255
PHONE: (205) 322-4197
FAX: (205) 322-2131

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GENE WEHLING

October 4, 1994

Rev. Marge Ragona
Covenant Metropolitan Community Church
P.O. Box 101473
Birmingham, AL 35210

Dear Rev. Ragona,

On behalf of the staff and clients of Birmingham AIDS Outreach, please accept our thanks for your donation of on 9-26-94. During the coming months we will be serving larger numbers of clients and without the continued generosity and support of people like you, we would not be able to meet those needs.

Sincerely,

Sam Thompson
Executive Director

Questions



VOLUME 5
Number 2
1994

Questions About...Drug Development and Approval

On average, it takes 12 years and \$231 million to get one new medicine from the laboratory to the pharmacist's shelf. Only five in 4,000 compounds screened in pre-clinical testing make it to human testing. One of these five tested in people is approved. The research-based pharmaceutical industry will invest \$10.9 billion in research and development this year, and that investment has been doubling every five years. Following are questions about the steps that must be taken for a drug to be approved.

1. What is Preclinical Testing?

Laboratory and animal studies are performed to show biological activity against the targeted disease, and the compounds are evaluated for safety. These tests take approximately three and one-half years.

2. What is an Investigational New Drug Application (IND)?

After completing preclinical testing, the company files an IND application with the FDA to begin to test the drug in people. The IND becomes effective if the FDA does not disapprove it within 30 days. The IND shows results of previous experiments; how, where, and by whom the new studies will be conducted; the chemical structure of the compound; how it is thought to work in the body; any toxic effects found in the animal studies; and how the compound is manufactured. In addition, the IND must be reviewed and approved by the Institutional Review Board where the studies will be conducted, and progress reports on clinical trials must be submitted at least annually to the FDA.

3. What are Phase I Clinical Trials?

These tests take about a year and involve about 20 to 80 normal, healthy volunteers. The tests study a drug's safety profile, including the safe dosage range. The studies also determine how a drug is absorbed, distributed, metabolized and excreted, and the duration of its action.

4. What are Phase II Clinical Trials?

In this phase, controlled studies of approximately 100 to 300 volunteer patients (people with the disease) assess the drug's effectiveness and take about two years.

5. What are Phase III Clinical Trials?

This phase lasts about three years and usually involves 1,000 to 3,000 patients in clinics and hospitals. Physicians monitor patients closely to determine efficacy and to identify adverse reactions.

6. What is a New Drug Application (NDA)?

Following the completion of all three phases of clinical trials, the company files an NDA with the FDA if the data successfully demonstrates safety and effectiveness. The NDA must contain all the scientific information that has been gathered. NDAs typically run 100,000 pages or more. By law, the FDA is allowed six months to review the NDA. In almost all cases, the period between the first submission of an NDA and final FDA approval exceeded that limit; the average NDA review time for new molecular entities approved in 1991 was 30.3 months.

7. Is There an Expedited Process?

Under a plan implemented by the FDA in 1989, Phases II and III may be combined to shave two to three years from the development process for those medicines that show sufficient promise in early testing and are targeted against serious and life-threatening diseases, such as AIDS.

8. What Follows Approval?

Once the FDA approves the NDA, the new medicine becomes available for physicians to prescribe. The company must continue to submit periodic reports to the FDA, including any cases of adverse reactions and appropriate quality-control records. For some medicines, the FDA requires additional studies to evaluate long-term effects.

Lee Howell, M.D.
Administrator
UAB AIDS Center

UAB AIDS Center Update

National Mucosal Immunology Laboratory

A grant awarded last summer to Jiri Mestecky, M.D., recognizes that the University of Alabama at Birmingham is on the cutting edge of research in mucosal immunity. The Central Mucosal Immunology Laboratory has been established here to investigate mucosal responses in human AIDS vaccine trials.

Further grants from the National Cooperative Vaccine Development Group for AIDS have established UAB as a national site for mucosal immunology testing. The Central Mucosal Immunology Lab here will support the work of all six of the national AIDS Vaccine Evaluation Units (AVEUs).

"Last year the National Institutes of Health (NIH) established the Mucosal Immunology Laboratory at UAB as a component of the national AVEU program to determine the potential of new vaccines designed to induce immune responses and protective immunity at the most common sites of entry of HIV of the genital and lower intestinal tracts," Dr. Mestecky explains.

The National Institute of Allergy and Infectious Diseases (NIAID) AIDS Vaccine Evaluation Group (AVEG) includes the AVEU based at UAB as well as two immunology laboratories, a statistical coordinating center, and a central specimen repository—all of which support the clinical trials effort of the AVEU.

Of the more than two dozen potential AIDS vaccines that have been or are currently being tested in humans worldwide, AVEG has initiated 17 trials with 13 of these products. AVEG pioneered the first Phase II trial of two HIV vaccines, the first trial of an HIV peptide vaccine, and the first trial of an oral HIV vaccine (now enrolling at UAB).

UAB has one of the largest research groups in the country working on the AIDS virus and a series of associated vaccines. Investigators here are particularly known for their work with mucosal and systemic immune responses to infectious agents, including HIV. This is critically important in light of the fact that studies show that at least 80 percent of all HIV is transmitted by sex or from infected mothers to their babies—modes of transmission that involve mucosal membranes.

Patricia Fast, M.D., Ph.D., chief of the Clinical Development Section of the Vaccine Research and Development Branch within NIAID's Division of AIDS, comments, "We are excited by the addition in Birmingham. Their expertise in mucosal immunity is well known and critically important for designing an effective AIDS vaccine."

Center for AIDS Research Award Renewed

The AIDS Center Research/Core Support Grant was renewed by the National Institutes of Health (NIH) in March 1994 for an additional five years with a priority score of 0.1 percent—the highest priority score of any Center for AIDS Research in the country. This score places UAB ahead of such prestigious institutions as the University of California at San Francisco, Duke University, Dana-Farber Cancer Institute, New York University, and the University of Washington in Seattle.

"We have been very fortunate to have the generous support of UAB during the evolution of our Center," says Lee Howell, M.D., administrator of the UAB AIDS Center. "The commitment of our parent institution is nothing short of outstanding. The amount and quality of the space, as well as the designation of the Center as a separate department, underscore the value that UAB places on our Center. The renewal of the Center grant will allow us to continue our mission of promoting research and training in AIDS and related diseases."

The renewal funds six specialized core facilities, a developmental grant program, and recruitment, as well as some support for administration of the Center. In addition, the grant will fund a new Biostatistics Core, which will provide data management services to support the research programs and projects conducted by the members of the AIDS Center.

The success of UAB's AIDS program is reflected in the dramatic growth in funding for AIDS-related research—from approximately \$4 million in 1988 to \$14.6 million (current year direct cost) in 1994, according to Eric Hunter, Ph.D., director

Study Update: Current AIDS Clinical Research

The UAB AIDS Center is currently enrolling patients for clinical trials. The following trials sponsored by the Alabama AIDS Vaccine Evaluation Unit (AVEU) of UAB are for HIV-negative persons willing to participate in the trials testing AIDS vaccines. Interested individuals should contact Rick Meriwether or Brenda Hunter at (205) 975-2838 or toll free 1-800-822-8816 for information.

AVEG 018

A trial of a preventive AIDS vaccine for HIV-negative volunteers. The vaccine is a synthetic protein to be administered orally. One year follow-up.

AVEG 019

A trial of a candidate preventive AIDS vaccine (p24VLP) delivered by injection and by mucosal routes. Volunteers needed; 18 years of age or older; HIV-negative.

This section lists the current clinical trials being conducted at the UAB AIDS Center's 1917 Research Clinic. If you would like further information on any of these trials, please call the 1917 Research Clinic at 934-3690, or if you are calling outside the local area, call UAB HealthFinder at 1-800-822-8816 and ask for the 1917 Research Clinic.

ACTG 177

A study of TB prophylaxis. Patients will receive INH, PZA, and rifampin. To be eligible for participation, patients must have positive PPD and no active TB.

ACTG 193A

A study to compare 4 nucleoside regimens in advanced HIV patients involving ddI, ddC, AZT, and nevirapine. To be eligible for participation, patients must have a T4-cell count < 50.

ACTG 242

A study to evaluate amitriptyline and mexilitine for painful neuropathy. Patients will need a positive viral culture or p24 antigen.

ACTG 259

A phase II study of SC-49483 in combination with AZT versus AZT alone. To be eligible for participation, patients must have a T4-cell count of 50-350 and < 6 months prior AZT therapy.

ACTG 159/MSG 17

A study of cryptococcal meningitis acute therapy to compare amphotericin B with and without 5FC, then maintenance drug with itraconazole or fluconazole.

MSG 30

A study of itraconazole- or fluconazole-resistant oral thrush to evaluate efficacy and safety of itraconazole oral solution.

PHA 008

A time intensive study of filgrastim (G-CSF) for neutropenia. Patients must have a T4-cell count < 200.

PHA 015

A study of Abbott protease inhibitor to evaluate antiviral activity and safety. Patients must have a T4-cell count 50-500.

PHA 013

A study of delavirdine and AZT vs. AZT alone. Patients must have T4-cell count 200-500.

ACTG 228

A study of CMV retreatment to evaluate safety and efficacy of 3 regimens for CMV retinitis. Patients must have active CMV, have received gancyclovir or foscavir in past 28 days, and have neutrophil count > 500.

PHA 012

A 26 week trial of oral gancyclovir for maintenance treatment of CMV retinitis.

PHA 016

A study of Merck protease inhibitor in combination with AZT and ddI to evaluate safety and efficacy of combination therapy. Patients must have a T4-cell count < 500.

ACTG 251

A study of thalidomide for treatment of oral aphthous ulcers.

ACTG 261

A phase II study of delavirdine in combination with AZT and ddI. Patients must have < 6 months prior to AZT therapy and a T-cell count of 150-350.

This next section, which is particularly concerned with pregnant women, infants, and children, lists trials currently being conducted at the UAB AIDS Center's Family Clinic at The Children's Hospital. For details of these trials, please call 939-9400, or if you are calling outside the local area, call UAB HealthFinder at 1-800-822-8816 and ask for the Family Clinic at Children's Hospital.

ACTG 219

This natural history study is designed for observation and follow-up of HIV-infected adolescents who have been or are currently enrolled in ACTG protocols.

ACTG 220

This study is for HIV-infected adolescents between the ages 13 and 20 and is designed for observation and follow-up of adolescents prior to the need for treatment.

ACTG 239

A Phase I/II study to evaluate the safety, toxicity, and effectiveness of AZT versus combination therapy with AZT

and ddI in young infants with HIV infection. Patients must be > 180 days of age.

ACTG 240

A randomized comparative trial of AZT versus d4T in children with HIV infection. Patients must be 90 days to 6 years of age and have less than 6 weeks of antiretroviral therapy.

ACTG 245

A comparative study of combination antiretroviral therapy in children and adolescents with advanced HIV disease. Patients must be between 6 months and 20 years of age and have had at least 24 weeks of prior antiretroviral therapy.

Alabama's AIDS Vaccine Evaluation Unit

In September, researchers at the University of Alabama at Birmingham's new AIDS Vaccine Evaluation Unit (AVEU) began enrolling volunteers into trials of potential AIDS vaccines.

Mark Mulligan, M.D., director of Alabama's AVEU and associate professor of medicine and microbiology at UAB, was awarded an NIH grant in May for the establishment of this research center, which will broaden the vaccine-development effort with human clinical trials. The Alabama AVEU is one of six such units in the country that have been awarded contracts by the National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID) to test a range of preventive vaccines aimed at bolstering the immune system's response to the HIV virus.

Mulligan says that there is absolutely no danger of acquiring HIV infection from the vaccines themselves, which are created with synthetic proteins that structurally mimic the AIDS virus's outer coat.

"The vaccines are made in the laboratory," Mulligan explains. "They're created with synthetic proteins that look like a protein that exists on the surface of HIV. However, the vaccines do not contain any part of the virus, they didn't come from the virus, and they contain no viral DNA. Because they're not killed virus or live virus, there's absolutely no possibility of acquiring HIV infection from the vaccine.

"We hope that these protein 'mimics,' which are administered to the volunteer as a vaccine, will appear to the body's immune system to look like HIV, and the immune system will then produce antibodies and T-cells," says Mulligan.

These studies are Phase I and II trials—the early phases of testing. "We're mainly looking at safety and immune response in these studies," Mulligan notes. "We're not really looking, at this point, to see if the vaccines prevent infection. If a vaccine looks promising in our studies, it will later be put into a much larger, Phase III, efficacy trial. Our current studies will involve dozens of people. The Phase III efficacy trials will involve thousands of people, all in high-risk groups."

Mulligan expresses hope that an effective AIDS vaccine will be developed "within the next decade." The co-directors of the Alabama AVEU are Drs. Jiri Mestecky

and Edward Hook, III. Mucosal membrane immune responses will be studied in depth at UAB, since over 80 percent of HIV transmission occurs across the body's mucosal surfaces.

As recipient of a five-year NIAID contract with first-year funding of \$1.3 million, the Alabama AVEU represents a major advance in the battle to create vaccines that work successfully against more than just two or three of the hundreds of strains of HIV. Over the course of five years, a range of the most promising vaccines will be tested on approximately 150 HIV-negative volunteers every year. Most of the vaccines will be administered in three separate doses, and volunteers will undergo regular blood draws after immunization, so that researchers can determine if the body is responding as hoped to the vaccine. Potential volunteers should be males or females, ages 18 and over, and HIV-negative and may call 975-2838 (or toll-free at 800-822-8816) for more information.

—By Barbara Westlake-Kenny

Research Award from pg. 2

of UAB's federally designated Center for AIDS Research. Even more impressive is the total current year direct cost funding for UAB AIDS Center investigators—approximately \$32.5 million and total current year funding (direct and indirect) for Center investigators which is over \$43 million—a figure that represents nearly a quarter of UAB's extramural funding.

"Through high-quality, multidisciplinary research, UAB has pioneered many breakthroughs in dealing with the AIDS epidemic," Hunter says. UAB boasts one of the largest research groups in the country working on the AIDS virus and associated diseases. Among other advances, UAB investigators played critical roles in developing new vaccines aimed at protecting against sexual transmission of the virus and demonstrating the vaccines' effectiveness in animals. UAB scientists were also the first to demonstrate that persons recently infected with the AIDS virus have high levels of virus circulating in the blood and that by developing sensitive methods to detect the virus, it is possible to rapidly assess the antiviral activity of new AIDS drugs.

—By Barbara Westlake-Kenny

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No Casual Transmission of HIV

Recently, there have been documented reports of transmission of HIV from one infected household member to another. Although the mode of transmission was not definitively identified, all of these cases most likely involved an undocumented exposure of the virus to skin lesions that may have facilitated transmission. In the case of two adolescent brothers with hemophilia, transmission most likely occurred during an episode of razor-sharing. Despite these reports, seventeen previous studies in the United States and Europe have examined the prevalence of HIV infection among non-sexual, non-needle sharing household contacts of person with HIV infection; none of the 1167 contacts who were followed for more than 1700 person-years in these studies were infected. The findings of these reports reemphasize the need for standard precautions to prevent contact with blood in households and other settings. In homes, schools, and day-care centers, children may live, learn, and play with children who have HIV infec-

tion or whose HIV-infection status is unknown. Because the risk of transmission in these settings is extremely low, HIV-infected children should not be excluded solely on the basis of their infection. Persons caring for children should be trained in, and adhere to, proper infection-control techniques. As the HIV epidemic continues into its second decade, cases of transmission in unusual settings will be recognized. Adherence to guidelines for preventing blood exposure will reduce the risk for blood contact even in homes and other settings in which the risk is already extremely low.

Sources:

New England Journal of Medicine,
December 16, 1993.

Morbidity and Mortality Weekly Report,
December 17, 1993.

Lee Howell, M.D.

Administrator
UAB AIDS Center

HIV Treatment News

AZT in Pregnancy Prevents HIV Infections in Babies

Each year in the United States, four million women give birth. About 7,000 of these women are HIV-infected. Without treatment, approximately 2,000 of their babies will acquire HIV infection from their mothers. However, important new results from a study of 477 HIV-infected pregnant women and their newborn babies has found that the drug AZT dramatically reduces transmission of HIV from infected mothers to their newborns. This good news has major public health importance.

In the new study (ACTG 076 sponsored by the U.S. National Institutes of Health and the French government), 26 percent of women who received placebo passed the virus to their babies. Among babies born to mothers who received AZT in the study, only 8 percent became infected with HIV. These babies

also received AZT for six weeks after birth. After an 18 month follow-up, there were no differences in birth defects among infants in the AZT or placebo groups.

The finding that AZT in pregnant women and their newborns can reduce HIV infections among newborns by approximately two-thirds is considered highly significant. Pregnant women with HIV infection and their physicians should discuss the benefits and potential risks of AZT treatment.

Source:

Morbidity and Mortality Weekly Report,
August 5, 1994

Mark J. Mulligan, M.D.

Editor-In-Chief

Support groups lead to positive attitudes

Testing positive for HIV infection does not mean an individual is about to die. This is an illness that can be treated; while we may not be able to cure this disease at this time, treatment permits an individual to live a relatively prosperous and healthy life for a number of years. Many long term survivors attribute their ability to live with the virus to a positive mental attitude and the support of friends, partners, or relatives who demonstrate love and concern. The mission of Birmingham AIDS Outreach (BAO) is to assist where we can in improving the quality of life for those affected by HIV and AIDS. Our support groups are a major component in meeting this mission. These groups are open to anyone affected by this disease.

The support groups sponsored by BAO include specific groups for surviving family members and partners, care givers, persons living with AIDS, women, and a new group for individuals recently diagnosed with HIV. Several groups meet at BAO, while others meet at other locations. The last Wednesday night of every month is devoted to a program called Positive Attitudes. During this time, various speakers and presenters discuss

positive ways for living with HIV. A quote from a poem by Peter Ackerman sums up the agency philosophy regarding this disease:

*I refuse to believe or accept that
because I am affected by AIDS
that I am doomed and hopeless,
that my life is defined
by death.*

*I am no less a person because
I have AIDS.
Having AIDS doesn't lower
my worth as a human being,
nor shall I let it deprive
me of my
needs.*

**For further information about
support groups, contact the
BAO office at (205) 322-4197.**

**Sam Thompson
Executive Director
Birmingham AIDS Outreach**

Questions

BAO
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550070
Birmingham, AL
35255

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BIRMINGHAM AL 35209

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A Questions & Answers

What is the cost to Business of HIV?

According to a Blue Cross and Blue Shield Association study, employees with HIV will cost medium and large businesses an average of \$16,639 over five years. This cost includes money spent on health insurance, disability payment, and training of replacements. The Centers for Disease Control estimates that the lifetime cost of caring for someone with AIDS is \$100,000. The Blue Cross estimate is so low because of a 66 percent chance that employees with HIV will not develop AIDS within five years.

Source: Positively Aware, Summer, 1994.

Is a home test available to test for HIV infection?

The FDA is considering two kinds of kits: the Direct Access kit, which would allow an individual to produce an analyzable blood sample and send it to a lab, and the true home testing kit, which would allow an individual to test him or herself and determine the result. Most people learn of their HIV status by a doctor or other clinic worker which provides the opportunity to ask questions and receive counseling. The Direct Access kit will provide counseling during telephone contact with a counseling center; a true home-testing kit might not. Sole reliance on printed materials for counseling may be inadequate, since a pamphlet can't respond to questions and may be written in language the test-taker doesn't understand.

Source: POZ, Vol 1:2, June/July, 1994

*If you have a question you
would like answered in this
column, please write to
the following address:
Questions & Answers
UAB AIDS Center
256 BBRB UAB Station,
Birmingham, AL 35294*

RUNNING WITH THE ANGELS

by
Bobbie Stasey

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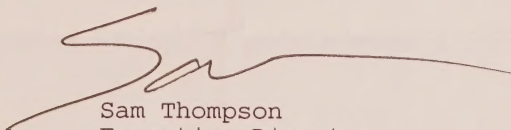
October 4, 1994

Rev. Marge Ragona
Covenant Metropolitan Community Church
P.O. Box 101473
Birmingham, AL 35210

Dear Rev. Ragona,

On behalf of the staff and clients of Birmingham AIDS Outreach, please accept our thanks for your donation of \$80.00 on 8-29-94. During the coming months we will be serving larger numbers of clients and without the continued generosity and support of people like you, we would not be able to meet those needs.

Sincerely,



Sam Thompson
Executive Director

Thank you for registering to be a part of the crowd of enthusiastic men, women and children who will walk together to fund the fight against AIDS by raising money for AIDS education, care and services.

1. Congratulations! You are a registered walker for the third annual Aalabama AIDS Walk. If you need further information about the Walk or Birmingham AIDS Outreach please call (205) 322-4197.

2. Form a team! Any five or more people can walk together and qualify as a team. Walk in honor of someone living with HIV or walk in memory of someone who has died from AIDS. Ask your employer to show support by forming a company team.

3. Get sponsors! Ask your family, friends, neighbors, co-workers, and the businesses you frequent to sponsor your walk for life. Collect donations in advance to turn in the day of the walk! Any amount is appreciated. Prizes will be awarded for the following amounts raised:

\$25 Drink Hugger
\$50 Billed Sport Cap
\$100 Walk T-shirt
\$200 Handy Lunch Cooler
\$350 Picnic Cooler Bag
\$500 Sport Duffel Bag
\$1,000 Walk Jacket

The Grand Prize to the top person who raises the most money is a fabulous three day, two night trip for two to any city in the continental U.S. Round trip air travel and hotel accommodations are courtesy of Marco Polo of the Carlson Travel Network.

Drink huggers, T-shirts and caps will be available the day of the walk (first come, first served for the first 1,500 qualifiers). All other incentives will be available in 4-6 weeks.

4. Walk on Sunday, October 23!

Come rain or shine, we will gather at the UAB Mini-park at the corner of 8th Ave. So. and 14th St.. UAB lots will be available for free parking.

Schedule of Events

12:00pm Registration opens
Live entertainment begins
Food vendors open
2:00pm.....Warm-up stretching and aerobics
3:00pm.....Opening Ceremony
4:30pm Closing Ceremony
Recognition and appreciation
awards announcements.

**Bring This Packet With You
to the Walk.**



Alabama AIDS Walk

Sunday, October 23, 1994

UAB Mini Park



Sponsored by
Birmingham AIDS Outreach
P.O. Box 550070, Birmingham AL 35255
(205)322-4197

Name _____

Mailing Address _____

City_____ State_____ Zip_____

Employer _____

Team Name: _____ **Name of Team Leader:** _____

50% to go to Birmingham AIDS Outreach and 50% to go to (please designate one HIV/AIDS agency only) _____

Amount of contribution

\$10	\$25	\$50	\$75	\$100	Other
------	------	------	------	-------	-------

[illegible]

Subtotals	+	+	+	+	+	=
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Additional list of contributions included in this envelope ____Yes ____No.

Grand Total

In consideration of the advancement of your purposes, objectives and work, and in consideration of your organization permitting me to participate in the "For All Walks of Life" Alabama Walk for AIDS, on behalf of myself, my heirs, my guardians, executors, administrators or assignees including attorney's fees and court costs (collectively "Claims"). I hereby waive and release any and all rights and claims for damages which I may have against you, as well as any other person connected with the "For All Walks of Life" Alabama Walk for AIDS, their heirs, executors, administrators, successors and assignees for any and all injuries which may result directly or indirectly from my participation. I further state that I am in proper physical condition to participate in this event. I also give permission for the use of my name and/or picture in any broadcast, telecast, or other account of this event.

X _____
Walker's signature

X
Parent/Guardian Signature for Walkers Under Age 18

Sample letter you can
write, copy + distribute
to get donations.

Dear Neighbor,

I will be walking to fight AIDS
in the 1994 Alabama AIDS Walk
on Sunday, Oct. 23rd.

My personal mission is to collect
as much money as possible between
now and the walk to help
in the fight against this killer
virus. HIV/AIDS is now fastest
growing in our heterosexual popu-
lation, especially in our youth.

Only money for education can
help stop this epidemic!

Please sponsor me in my efforts.
Send a check made out to Birmingham
AIDS Outreach (BAO) to me: Julie
Sampson, 2076 Lakewood Drive, Birmingham,
AL 35216; or call me at 823-5769
and I'll come by and pick it up.
Do it NOW - HELP fight HIV/AIDS!

Sincerely
Julie Sampson

TEN HOT TIPS FOR FILLING UP YOUR DONATIONS ENVELOPE *

1. Set a personal goal for the amount of money you would like to collect.
2. Ask at least one person per day to sponsor you.
3. Set aside two hours a week to ask people to sponsor you.
4. Use high-tech voice mail, E-mail, computer networks, etc., to get the word out that you are looking for sponsors.
5. Write to your friends, your family, your holiday card list. (See attached sample of personal letter.)
6. Put up a notice at work or school.
7. Ask members of your church or clubs to which you belong if they will sponsor you.
8. Form a team to walk together and support each other in getting donations.
9. Put a walk message on your home answering machine.
10. Hold a walk house party.

* Attention Team Captains: Please copy this and distribute, along with donation envelopes to all team members.

Birmingham AIDS Outreach
Alabama AIDS Walk
P.O. Box 550070
Birmingham, AL 35255
(205) 322-4197

Alabama AIDS Walk 1994

INFORMATION PACKET

*"Walk with us so others won't
have to walk alone."*

Sponsored By:
Birmingham AIDS Outreach
P.O. Box 550070
Birmingham, AL 35255
(205) 322-4197

Dear Walk Volunteer:

Congratulations and thank you for participating in the 3rd annual Alabama AIDS Walk. Enclosed is a donation envelope with information about the Walk. If you need more envelopes, call the Walk Task Force at Birmingham AIDS Outreach, 322-4197.

We hope you are looking forward to the Walk on October 23rd. The money which is raised will benefit people affected by HIV disease throughout Alabama.

Here is everything you have always wanted to know about the Alabama AIDS Walk and more. We have made it brief and to the point. If you have questions after reading this packet, please call the Walk Task Force at Birmingham AIDS Outreach. We appreciate your participation and look forward to walking with you.

THE WALK:

The Alabama AIDS Walk is the largest annual fundraising event for BAO. Last year, over 5,000 walkers participated in the event and raised over \$110,000.00 for AIDS organizations throughout the state. The Walk encourages people from "all walks of life" to come together to promote community awareness about HIV and AIDS.

One hundred percent of the money you raise can go to BAO, or you can choose to give 50% of your money to BAO and 50% to one of the following organizations.

AIDS Task Force of Alabama (ATFA) - Birmingham, AL
A Baby's Place
Jefferson County AIDS in Minorities (AIM)
1917 Clinic - UAB
Family Clinic - Children's Hospital - UAB
HIV/AIDS Clinic - VA Hospital
St. George's Clinic - Cooper-Green Hospital
AIDS Action Coalition (AAC) - Huntsville, AL
AIDS Service Center (ASC) - Anniston, AL
West Alabama AIDS Outreach (WAAO) - Tuscaloosa, AL
Castlehill Clinic - Tuscaloosa, AL
Wiregrass AIDS Outreach - Dothan, AL
Lee County AIDS Outreach (LCAO) - Auburn, AL
Montgomery AIDS Outreach (MAO) - Montgomery, AL
Mobile AIDS Support Services (MASS) - Mobile, AL
Children's AID Society - Family Pairs Program
AIDS Research Center - UAB
AGAPE House - Birmingham, AL
Project Open Hand - Atlanta, GA

and other AIDS Service Organizations serving the citizens of the state of Alabama.

WHERE? WHEN? WHAT TIME?

The Alabama AIDS Walk will be held on Sunday, October 23, 1994. The Walk will begin and end at the UAB Mini-Park. Registration and entertainment begins at 12:00 noon, stretching and aerobics at 2:00 p.m., opening ceremony at 3:00 p.m. and awards ceremony at 4:30 p.m.

STARTING UP:

Starting up is easy! First decide if you want to be an individual walker or a team walker. The Team approach is the most fun! In order to walk as a team, you must choose a Team Captain.

WHAT IS A TEAM CAPTAIN?

A Team Captain is a walker who is responsible for recruiting other walkers through contacts with friends, relatives, his or her business, clubs, groups, etc.

TEAM CAPTAIN RESPONSIBILITIES:

1. Team Captains are responsible for recruiting walkers.
2. Team Captains are responsible for distributing posters, donation envelopes, and company newsletter articles. (See attached sample of company memo.)
3. Team Captains are encouraged to put up walk posters at work, school, church, etc. (Posters are available through BAO.)
4. Team Captains are encouraged to put articles about the Walk in organizational newsletters. (See attached sample of company announcement/newsletter article.)
5. Team Captains should be dedicated to recruiting as many people as possible and to helping team members get donations. Copy and distribute as much of this packet as you would like to get your team members started.
6. Team Captains are encouraged to write thank-you notes to team members.
7. Team Captains are responsible for whatever banners, signs, T-shirts, etc., that their team may want to use on the day of the Walk.

BUILDING YOUR TEAM:

Once you have a Team Captain, you can start building your team. You can do it in a highly organized fashion by asking several key people in your organization to meet with you as a committee, formulate some recruitment ideas, and hold an internal kick-off meeting. Or more simply, you can just put up posters with your extension number on them and wait for the calls! When someone calls about the Alabama AIDS Walk, give them a donations envelope. Soon the word will spread and your team will grow.

If you are forming a company team, you might want to involve management in the team member recruiting process. You can suggest to management that they form a team to challenge an employee team. You can also ask management to provide matching company T-shirts as an incentive to "show the company colors" at the Walk.

The spirit of teamwork is one that can do anything from winning SEC Championships to helping raise money for people affected by HIV and AIDS. Don't be afraid to start. Remember, every team begins with just one member!

INTERNAL/EXTERNAL PROMOTIONS:

Ideas for Internal Promotion - (1) When individuals register, put their names on a large poster on a main wall in the company. It's always great to see who else is walking. (2) Mini newsletters produced in your department are a great way to inform walkers of their team's progress. (3) Maybe the company will put a payroll stuffer in everyone's pay envelope to help get the ball rolling.

Ideas for External Promotion - (1) Send a news release to your local media about what your company's employees are doing to help the Alabama AIDS Walk and Birmingham AIDS Outreach, to help those affected by HIV and AIDS. (See attached sample press release) (2) Have a kickoff event with everyone meeting in front of your building for five minutes before or after work for a group picture in T-shirts.

DAY OF EVENT:

Organize before you go to the Walk. Tell your team members a specific time and place to meet at the mini-park. Be sure to have your team identification. Some teams wear T-shirts, some bring banners and signs, and some bring balloons. Make sure everyone at the Walk knows your team.

On the day of the walk, there will be entertainment for all ages. Food and merchandise vendors, face painting, a moon walk and several different musical groups are just a few examples.

Alabama AIDS Walk incentives will be given to walkers on the day of the event. Incentives will be given according to the amount raised as follows:

\$25	Beverage Hugger
50	Billed Sports Cap
100	Commemorative T-shirt
250	Lunch Cooler
500	Light Weight Sport Carry All
1000	Commemorative Jacket

The person raising the most money will receive a round trip air travel and hotel accommodations for two, to any city in the continental U.S. This fabulous trip is compliments of, Marco Polo, of the Carlson Travel Network in Homewood.

Good Luck!!

SAMPLE COMPANY ANNOUNCEMENT/NEWSLETTER ARTICLE

ALABAMA AIDS WALK TEAM CAPTAIN NAMED

_____ NAME _____ of _____ DEPARTMENT _____ has been designated as Team Captain for _____ COMPANY _____ for the Alabama AIDS Walk, scheduled for Sunday, October 23, 1994.

" _____ COMPANY _____ will be well represented in the Walk" said Team Captain _____ NAME _____. ["I'm planning for a large increase in the effort this year." or "It will be quite a challenge, but our employees are up to it. We'll be ready."]

Each Team Captain recruits fellow employees to participate in the 2.5 mile walk. They, in turn, obtain sponsors who back them with contributions for their participation. Last year over 5,000 people in Birmingham, walked together to help raise funds for education, direct care, and services to people affected by HIV.

Sign up now! To join your Alabama AIDS Walk Team, contact _____ NAME _____ at _____ PHONE # _____. For further information, you may also contact the Walk Task Force at Birmingham AIDS Outreach at 322-4197.

SAMPLE COMPANY MEMO

TO: All Personnel

RE: The Alabama AIDS Walk Challenge

As a Team Captain for our company's participation in the 1994 "For All Walks of Life", Alabama AIDS Walk, I want everyone to understand my goals for this event.

First, we are going to have FUN! We are going to build the most colorful, most energetic, most well-supported, most enthusiastic Team ever!

Second, we are going to knock the socks off of _____ Company. We're going to get more donations and field more walkers to help in the fight against AIDS. Our enthusiasm will help us get more relatives, friends and colleagues to form a bigger team. We beat 'em in sales last month; let's beat 'em in the Alabama AIDS Walk on Sunday, October 23.

So, if you're not already signed up to participate in the Walk, call me at extension _____. We need walkers. We can let Birmingham know that _____ Company is clearly the best, biggest and brightest Team anywhere! Remember, all proceeds will benefit Birmingham AIDS Outreach in its efforts to improve the quality of life for people affected by HIV through direct services, advocacy, and education.

HISTORY OF BIRMINGHAM AIDS OUTREACH

(This would be a nice addition to a press release, newsletter article or memo.)

In the latter part of 1984, Birmingham's gay helpline began receiving calls about a new disease, sometimes called ARC. In May, 1985, the leaders of the gay and lesbian community of Birmingham met to discuss how to respond to a crisis in the community associated with this disease, now referred to as AIDS. Out of that meeting a volunteer organization referred to as Birmingham AIDS Outreach (BAO), was formed. BAO's mission is to improve the quality of life for people affected by HIV through providing direct services, advocacy, and education. In 1993 BAO provided direct services to more than 280 individuals and made information and education available to thousands more.

In Alabama, there are over 2,800 diagnosed cases of AIDS and an estimated 5,000 to 10,000 people infected with HIV, the virus that causes AIDS. Due to these alarming statistics, BAO will hold its 3rd annual walk-a-thon to raise money for education, direct care, and services to people affected by HIV disease.

SAMPLE "CHALLENGE LETTER"

Dear _____:

On behalf of the employees of ABC Corporation, I would like to challenge you and your employees to participate in the 1994 Alabama AIDS Walk for Birmingham AIDS Outreach (BAO).

The Alabama AIDS Walk is BAO's largest annual fund raiser. Company teams and individuals walk to raise funds for education, direct care, and services to people affected by HIV.

In past years, hundreds of our employees, including many in senior management, have participated in the Walk. It provides a cost-effective platform for some real team-building within the company. When executives and employees join together to take on the challenge of walking 2.5 miles, a strong bond is formed between them.

The Alabama AIDS Walk is also a great way to associate your company with an important cause - the prevention of HIV and AIDS. Accept this friendly challenge! Join ABC Company as we walk together, so that people affected by HIV do not have to walk alone.

Sincerely,

Chief Executive Officer

BIRMINGHAM AIDS OUTREACH

HIV/AIDS STATISTICS

It is critical that we educate everyone about how to prevent HIV infection and AIDS. You can take the stand in developing your community's response to the disease by participating in the 1994 Alabama AIDS Walk.

DID YOU KNOW?

One person is infected with HIV every 13 minutes.

AIDS is the leading cause of death among men between the ages of 25-44 in the U.S. One half of our nation's 121 million workers are in this age group!

More than two-thirds of companies with 2,500 to 5,000 employees and nearly one in 12 small employers have experienced an employee with HIV infection or AIDS.

It is estimated that one in every 250 people are infected with HIV, the virus that causes AIDS.

Of the one to two million individuals estimated to be infected with HIV in the U.S., 75% are unaware of their condition.

In the United States, 361,509 individuals have been diagnosed with AIDS.

AIDS is the sixth leading cause of death for young people (ages 15-24).

The number of new AIDS cases among U.S. teenagers is doubling every 14 months. During the past two years, the total number of teens and young adults (ages 13-24) diagnosed with AIDS increased by over 77.5%. Forty-four percent of teens (ages 13-19) with AIDS are female. Heterosexual transmission accounts for 50% of AIDS cases among females (ages 13-24).

There are 2,802 diagnosed AIDS cases and an estimated 5,000 to 10,000 people infected with HIV in Alabama.

In Alabama, 14% of AIDS cases are transmitted by heterosexual contact, which doubles the national average of only 7%.

In Alabama, AIDS cases are double the national rate of infection for women.

Over 221,000 people have died as a result of this disease.

YOU CAN MAKE A DIFFERENCE

2. **Start your Legwork...** As a leader you can get your company behind your effort and form your own company team. Ask the public relations or human resource manager about appointing someone to head up the team and get things organized. Recruit your friends, family, colleagues, athletic league teammates, to join you as walker team members
3. **Collect team donations...** Ask your employer, neighbors, and local businesses and churches to support you in your community effort with donations toward fighting AIDS.
4. **Join the leaders of your community** at the starting line...on a wonderful fall afternoon... walking for the good of all...taking steps to further AIDS education and broaden services to care for and help enrich the lives of those living with HIV/AIDS.

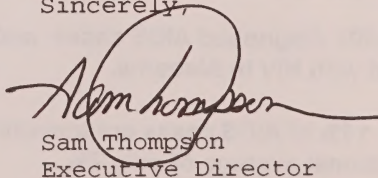
**You, and the people on your team are the key to our success...
And, you can be the key to saving a life!**

Start your company team now! Just complete the registration form and mail or fax it to us. We'll send your walker information packet right away. **Your packet will include...**

1. Generous sized envelopes, specially designed to help record and hold the donations collected by your team members,
 2. A tip sheet on how to recruit your team members,
 3. Helpful hints to get you started collecting donations so you can get as many of the great prizes as possible.
- and more!

Don't wait another minute! Join the thousands of Alabama leaders who have found community service to be fun, easy and personally fulfilling. Be a model for your family, friends, colleagues and employees. Register your company team today.

Sincerely,



Sam Thompson
Executive Director

P.S. Remember, with The 1994 AIDS Walk you can further AIDS education, care and services...earn prizes... enjoy a nice fall afternoon with your friends and family...and have a good time staying fit. And, if that's not enough...there will be live entertainment, clowns and face painting for the kids, and refreshments available for everyone!

P.S. Also, see AIDS Facts on the back of this page...
Join the Walk to reduce these statistics!

Sam Thompson
Executive Director

Announcing: The 3rd annual Alabama AIDS Walk
 Sunday October 23, 1994
 UAB Mini-Park
 For All Walks of Life...

You can get fit, have fun, and
 contribute to the well being of your community...

Feel good about yourself, and
 help others who desperately need it...and
 have a wonderful afternoon with your family, friends and
 associates...

Dear Community Leader,

If you're like most of us, you're very busy and often under great pressure. Your days are consumed with your work, your evenings filled with family, friends and more. There just never seems to be enough time.

Yet you strive for excellence. With all your duties to your career, family and friends, how can you possibly keep up with your community and civic responsibilities? You can't. Not by yourself.

Fortunately, there is a way for you
to contribute to the welfare of your community...
Participate in the 3rd annual Alabama AIDS Walk,
for AIDS education, care and services!

With the AIDS Walk, you and your family, friends and colleagues share a fantastic experience and bring each other up to speed in your civic contributions. Individual efforts are multiplied by the efforts of your team.

The Alabama AIDS Walk incorporates that concept and takes it further...You or someone in your organization can start developing your team by appointing someone in your organization (perhaps your public relations or human resources manager) to be the team leader and organizer; to put up posters, put articles about the Walk in your company newsletter; sign up team members, pass out information packets and generally keep things rolling.

Now you are on your way to having A REAL TEAM...



Alabama AIDS Walk

Sponsored by Birmingham AIDS Outreach, P.O. Box 550070, Birmingham, AL 35255
Phone (205) 322-4197 Fax (205) 322-2131

Each member of your team spends time in advance collecting donations from relatives, peers, classmates, church and civic friends, etc. They may know someone living with HIV or they may want to contribute in honor of someone who has died from AIDS. Local businesses, generous friends and neighbors will probably be glad to support you every step of the way toward fighting AIDS.

If you have walked with us in past years, you know you can have fun, stay fit, and help your community **by contributing to the AIDS education of the youth in your schools, churches and civic clubs. Further, you contribute to the care and quality of life of mothers, babies, teenagers and adults living with HIV/AIDS.**

In fact, you can even expand your business and social network while **you increase your community activity and well being.**

Get fit, have fun, and be a leader in your company and community...

You'll enjoy a wonderful fall afternoon walking with us so others won't have to walk alone.

And for the donations you collect from family and friends you get PRIZES...

☞...For collecting \$25 you'll get a cool cozy to keep your canned beverage "on ice" during those hot summer days,

and... ☞...For collecting \$50 you'll get a billed sports cap,

and a... ☞...Commemorative T-shirt for collecting \$100 in donations,

and a... ☞...Handy lunch cooler for \$250 in donations,

and a... ☞...Generous, sport carry all for collecting \$500,

and an... ☞ Attractive jacket for collecting \$1,000.

☞ **And... The Ultimate...**To the top person raising the most money the **Grand Prize is a fabulous trip!** You'll get **round trip air travel and hotel accommodations for two to any city in the continental U.S.** (3 days, 2 nights), compliments of Marco Polo Travel of the Carlson Travel Network.

It's so easy, you...

1. **Register Today...** Fill out the registration form. Send it in or fax it and we'll send you your official AIDS Walker information packet...